



## Clinical trial results:

### An Open-label, Non-controlled, Phase II Study to Evaluate the Safety, Pharmacodynamics, Pharmacokinetics, Efficacy and Conditions of Use of ARGX-113 in Patients with Mild to Moderate Pemphigus (Vulgaris or Foliaceus)

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2017-002333-40  |
| Trial protocol           | DE HU IT RO     |
| Global end of trial date | 28 October 2020 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 13 November 2021 |
| First version publication date | 13 November 2021 |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | ARGX-113-1701 |
|-----------------------|---------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03334058 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | argenx BV   |
| Sponsor organisation address | Industriepark Zwijnaarde 7, Zwijnaarde, Belgium, 9052 |
| Public contact               | Regulatory Manager, argenx BV, regulatory@argenx.com  |
| Scientific contact           | Regulatory Manager, argenx BV, regulatory@argenx.com  |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 28 October 2020 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 28 October 2020 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of efgartigimod in Pemphigus Vulgaris (PV) and Pemphigus Foliaceus (PF) subjects.

Protection of trial subjects:

This study was performed according to the International Conference on Harmonisation of Good Clinical Practice, the principles of the Declaration of Helsinki, and other applicable local ethical and legal requirements.

Background therapy:

Relapsing subjects under tapered prednisone therapy were kept in the study at the same dosage during the Induction treatment period. Then prednisone dosage could be tapered from the beginning of the Maintenance treatment period (Visit 5) up to study end (Follow-up Visit 3), according to standard of care (SoC). Newly diagnosed subjects or relapsing subjects off therapy, who were already on a first course of oral prednisone and for whom efgartigimod monotherapy was considered not clinically acceptable, were kept at the same dosage during the Induction treatment period. From the beginning of the Maintenance treatment period (Visit 5) up to study end (Follow-up Visit 3), prednisone dosage could be tapered according to SoC. Newly diagnosed subjects naïve to any treatment and relapsing subjects off therapy, or with a first course of oral prednisone ( $\leq 4$  weeks), for whom an initial period of efgartigimod monotherapy was judged clinically acceptable, were not administered any SoC (e.g. oral prednisone). Any adjuvant conventional immunosuppressant (e.g. mycophenolate mofetil, azathioprine) was discontinued at any time during the screening period.

SoC in additional Cohort 4:

- All subjects off therapy were associated with oral prednisone 20 mg/day at baseline. In relapsing subjects who were under oral prednisone therapy at tapered dose, oral prednisone was maintained at the same dosage, while any adjuvant conventional immunosuppressant was discontinued at any time during the screening period.
- Oral prednisone dose could be tapered as of end of consolidation (EoC) (the time at which no new lesions have developed for a minimum of 2 weeks, and approximately 80% of lesions have healed). For all subjects with a clinically active disease (e.g. worsening of the clinical signs) upon Investigator's judgment, a rescue treatment of oral prednisone could be implemented at any post-baseline visit.

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 02 November 2017 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Israel: 4   |
| Country: Number of subjects enrolled | Ukraine: 5  |
| Country: Number of subjects enrolled | Germany: 6  |
| Country: Number of subjects enrolled | Hungary: 11 |
| Country: Number of subjects enrolled | Italy: 8    |

|                                    |    |
|------------------------------------|----|
| Worldwide total number of subjects | 34 |
| EEA total number of subjects       | 25 |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 27 |
| From 65 to 84 years                       | 6  |
| 85 years and over                         | 1  |

## Subject disposition

### Recruitment

Recruitment details:

This Phase 2 study was conducted in subjects with mild to moderate PV or PF at 17 centers worldwide. Of the 53 subjects who were screened, 19 subjects were screen failures and 34 subjects were enrolled.

### Pre-assignment

Screening details:

The study comprised a screening period of up to 3 weeks, treatment periods ranging from 9 to 34 weeks, and a treatment-free follow-up period of 8 (Cohort 1) or 10 weeks (Cohorts 2-4).

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Non-randomised - controlled    |
| Blinding used                | Not blinded                    |

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | Cohort 1 (10 mg/kg) |

Arm description:

Efgartigimod intravenous (IV) 10 milligrams per kilogram (mg/kg) was administered as 4 weekly infusions during the induction period and during the maintenance period at weeks 2 and 6.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Efgartigimod          |
| Investigational medicinal product code | ARGX-113              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Efgartigimod (10 mg/kg), 250 milliliter (mL) was infused IV over a period of 2 hours. Subjects remained at the site for 2 hours minimum after the end of infusion during these visits as part of routine safety monitoring.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Cohort 2 (10 mg/kg) |
|------------------|---------------------|

Arm description:

Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period once every 2 weeks (q2w) for 8 weeks.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Efgartigimod          |
| Investigational medicinal product code | ARGX-113              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Efgartigimod (10 mg/kg), 250 mL was infused IV over a period of 2 hours. Subjects remained at the site for 2 hours minimum after the end of infusion during these visits as part of routine safety monitoring.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Cohort 3 (10 mg/kg) |
|------------------|---------------------|

Arm description:

Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period q2w for 12 weeks.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                       |
|--|-----------------------|
| Investigational medicinal product name | Efgartigimod          |
| Investigational medicinal product code | ARGX-113              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Efgartigimod (10 mg/kg), 250 mL was infused IV over a period of 2 hours. Subjects remained at the site for 2 hours minimum after the end of infusion during these visits as part of routine safety monitoring.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Cohort 4 (25 mg/kg) |
|------------------|---------------------|

Arm description:

Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC, and during the maintenance period q2w until Week 34.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Efgartigimod          |
| Investigational medicinal product code | ARGX-113              |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Efgartigimod (25 mg/kg), 250 mL was infused IV over a period of 2 hours. Subjects remained at the site for 2 hours minimum after the end of infusion during these visits as part of routine safety monitoring.

| <b>Number of subjects in period 1</b> | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) |
|---------------------------------------|---------------------|---------------------|---------------------|
| Started                               | 6                   | 5                   | 8                   |
| Completed                             | 3                   | 2                   | 7                   |
| Not completed                         | 3                   | 3                   | 1                   |
| Other                                 | 1                   | -                   | -                   |
| Investigator termination              | 2                   | 3                   | -                   |
| Withdrawal of informed consent        | -                   | -                   | 1                   |
| Lost to follow-up                     | -                   | -                   | -                   |

| <b>Number of subjects in period 1</b> | Cohort 4 (25 mg/kg) |
|---------------------------------------|---------------------|
| Started                               | 15                  |
| Completed                             | 10                  |
| Not completed                         | 5                   |
| Other                                 | -                   |
| Investigator termination              | 2                   |
| Withdrawal of informed consent        | 2                   |
| Lost to follow-up                     | 1                   |

## Baseline characteristics

### Reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | Cohort 1 (10 mg/kg) |
| Reporting group description:<br>Efgartigimod intravenous (IV) 10 milligrams per kilogram (mg/kg) was administered as 4 weekly infusions during the induction period and during the maintenance period at weeks 2 and 6. |                     |
| Reporting group title   | Cohort 2 (10 mg/kg) |
| Reporting group description:<br>Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period once every 2 weeks (q2w) for 8 weeks.                     |                     |
| Reporting group title   | Cohort 3 (10 mg/kg) |
| Reporting group description:<br>Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period q2w for 12 weeks.   |                     |
| Reporting group title   | Cohort 4 (25 mg/kg) |
| Reporting group description:<br>Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC, and during the maintenance period q2w until Week 34.                   |                     |

| Reporting group values                    | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) |
|---|---------------------|---------------------|---------------------|
| Number of subjects                        | 6                   | 5                   | 8                   |
| Age categorical<br>Units: Subjects        |                     |                     |                     |
| Age continuous<br>Units: years            |                     |                     |                     |
| arithmetic mean                           | 42.0                | 64.6                | 46.9                |
| full range (min-max)                      | 29 to 63            | 43 to 78            | 30 to 65            |
| Gender categorical<br>Units: Subjects     |                     |                     |                     |
| Female                                    | 3                   | 4                   | 7                   |
| Male                                      | 3                   | 1                   | 1                   |
| Ethnicity<br>Units: Subjects              |                     |                     |                     |
| Hispanic or Latino                        | 0                   | 0                   | 0                   |
| Not Hispanic or Latino                    | 6                   | 5                   | 8                   |
| Race<br>Units: Subjects                   |                     |                     |                     |
| White                                     | 6                   | 5                   | 8                   |
| Black or African American                 | 0                   | 0                   | 0                   |
| Asian                                     | 0                   | 0                   | 0                   |
| American Indian or Alaska Native          | 0                   | 0                   | 0                   |
| Native Hawaiian or Other Pacific Islander | 0                   | 0                   | 0                   |
| Multiple Race                             | 0                   | 0                   | 0                   |
| Pemphigus Type<br>Units: Subjects         |                     |                     |                     |
| PV: Mucosal-dominant                      | 1                   | 3                   | 3                   |

|                   |   |   |   |
|-------------------|---|---|---|
| PV: Mucocutaneous | 4 | 2 | 4 |
| PV: Cutaneous     | 1 | 0 | 0 |
| PF                | 0 | 0 | 1 |

| Reporting group values | Cohort 4 (25 mg/kg) | Total |  |
|------------------------|---------------------|-------|--|
| Number of subjects     | 15                  | 34    |  |
| Age categorical        |                     |       |  |
| Units: Subjects        |                     |       |  |

|   |          |    |  |
|---|----------|----|--|
| Age continuous                            |          |    |  |
| Units: years                              |          |    |  |
| arithmetic mean                           | 53.3     |    |  |
| full range (min-max)                      | 22 to 85 | -  |  |
| Gender categorical                        |          |    |  |
| Units: Subjects                           |          |    |  |
| Female                                    | 8        | 22 |  |
| Male                                      | 7        | 12 |  |
| Ethnicity                                 |          |    |  |
| Units: Subjects                           |          |    |  |
| Hispanic or Latino                        | 0        | 0  |  |
| Not Hispanic or Latino                    | 15       | 34 |  |
| Race                                      |          |    |  |
| Units: Subjects                           |          |    |  |
| White                                     | 14       | 33 |  |
| Black or African American                 | 0        | 0  |  |
| Asian                                     | 1        | 1  |  |
| American Indian or Alaska Native          | 0        | 0  |  |
| Native Hawaiian or Other Pacific Islander | 0        | 0  |  |
| Multiple Race                             | 0        | 0  |  |
| Pemphigus Type                            |          |    |  |
| Units: Subjects                           |          |    |  |
| PV: Mucosal-dominant                      | 2        | 9  |  |
| PV: Mucocutaneous                         | 4        | 14 |  |
| PV: Cutaneous                             | 2        | 3  |  |
| PF  | 7        | 8  |  |

## End points

### End points reporting groups

|  |                     |
|--|---------------------|
| Reporting group title  | Cohort 1 (10 mg/kg) |
| Reporting group description:<br>Efgartigimod intravenous (IV) 10 milligrams per kilogram (mg/kg) was administered as 4 weekly infusions during the induction period and during the maintenance period at weeks 2 and 6.  |                     |
| Reporting group title  | Cohort 2 (10 mg/kg) |
| Reporting group description:<br>Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period once every 2 weeks (q2w) for 8 weeks.  |                     |
| Reporting group title  | Cohort 3 (10 mg/kg) |
| Reporting group description:<br>Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period q2w for 12 weeks.  |                     |
| Reporting group title  | Cohort 4 (25 mg/kg) |
| Reporting group description:<br>Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC, and during the maintenance period q2w until Week 34.  |                     |
| Subject analysis set title   | Cohorts 1-3         |
| Subject analysis set type  | Full analysis       |
| Subject analysis set description:<br>Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period in Cohorts 1, 2, and 3; and during the maintenance period at weeks 2 and 6 (Cohort 1), q2w for 8 weeks (Cohort 2), and q2w for 12 weeks (Cohort 3).   |                     |
| Subject analysis set title   | Cohorts 1-4         |
| Subject analysis set type  | Full analysis       |
| Subject analysis set description:<br>Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period in Cohorts 1, 2, and 3; and during the maintenance period at weeks 2 and 6 (Cohort 1), q2w for 8 weeks (Cohort 2), and q2w for 12 weeks (Cohort 3). Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC in Cohort 4; and during the maintenance period q2w until Week 34. |                     |

### Primary: Number of Subjects who Experienced Treatment-emergent Adverse Events (TEAEs)

|   |   |
|---|---|
| End point title   | Number of Subjects who Experienced Treatment-emergent Adverse Events (TEAEs) <sup>[1]</sup> |
| End point description:<br>A TEAE was an undesirable event not present prior to medical treatment, or an already present event that worsened either in intensity or frequency following the treatment.<br>A serious adverse event (SAE), experience or reaction, was any untoward medical occurrence (whether considered to be related to investigational medicinal product [IMP] or not) that at any dose: <ul style="list-style-type: none"><li>• Resulted in death;</li><li>• Was life-threatening;</li><li>• Required in subject hospitalization or prolongation of existing hospitalization;</li><li>• Resulted in persistent or significant disability or incapacity;</li><li>• Was a congenital abnormality or birth defect;</li><li>• Medically significant events, which did not meet any of the criteria above, but may have jeopardized the subject and may have required medical or surgical intervention to prevent one of the other serious outcomes listed in the definition above.</li></ul><br>The Safety analysis set (SAS) included all enrolled subjects who received at least 1 dose of efgartigimod. |   |
| End point type  | Primary   |
| End point timeframe:<br>From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks   |   |



Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No additional statistical analysis was prespecified for this end point.

| End point values            | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) | Cohort 4 (25 mg/kg) |
|-----------------------------|---------------------|---------------------|---------------------|---------------------|
| Subject group type          | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed | 6                   | 5                   | 8                   | 15                  |
| Units: subjects             |                     |                     |                     |                     |
| TEAE                        | 6                   | 4                   | 6                   | 13                  |
| SAE                         | 1                   | 1                   | 0                   | 0                   |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Vital Sign Measurements

|                 |  |
|-----------------|--|
| End point title | Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Vital Sign Measurements <sup>[2]</sup> |
|-----------------|--|

End point description:

At each visit, vital signs (supine blood pressure, pulse rate, and oral body temperature) were assessed. Supine blood pressure and pulse rate were measured using standard equipment after approximately 10 minutes in a supine position.

The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

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

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No additional statistical analysis was prespecified for this end point.

| End point values            | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) | Cohort 4 (25 mg/kg) |
|-----------------------------|---------------------|---------------------|---------------------|---------------------|
| Subject group type          | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed | 6                   | 5                   | 8                   | 15                  |
| Units: subjects             | 1                   | 0                   | 0                   | 2                   |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Electrocardiograms (ECG)

|                 |   |
|-----------------|---|
| End point title | Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Electrocardiograms (ECG) <sup>[3]</sup> |
|-----------------|---|

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**End point description:**

ECG was taken at a paper speed of 25 millimeter/second and should be obtained with the subject in the supine position after they have rested in this position for at approximately 10 minutes. Three consecutive ECG recordings was taken with an interval of approximately 5 minutes at each occasion to obtain reliable and interpretable data. The ECG parameters that were collected are heart rate, PR, QRS, QT whereas QTcF was calculated.

The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

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

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**End point timeframe:**

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

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**Notes:**

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No additional statistical analysis was prespecified for this end point.

| End point values            | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) | Cohort 4 (25 mg/kg) |
|-----------------------------|---------------------|---------------------|---------------------|---------------------|
| Subject group type          | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed | 6                   | 5                   | 8                   | 15                  |
| Units: subjects             | 0                   | 0                   | 0                   | 0                   |

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**Statistical analyses**

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No statistical analyses for this end point

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**Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Physical Examinations (Cohorts 1-3)**

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|                 |   |
|-----------------|---|
| End point title | Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Physical Examinations (Cohorts 1-3) <sup>[4][5]</sup> |
|-----------------|---|

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**End point description:**

At each visit, physical examinations were carried out. Only physical examinations and visits where a clinically significant change from baseline occurred are included below. A clinically significant change from baseline was defined as a change from normal or abnormal (not clinically significant) to abnormal (clinically significant) post-baseline. The complete physical examination included an assessment of general appearance, skin, head and neck (including ears, eyes, nose and throat), lymph nodes, thyroid, musculoskeletal/extremities, abdomen, breast, and cardiovascular, respiratory, neurological, and genital/rectal systems.

The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

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

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**End point timeframe:**

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

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**Notes:**

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No additional statistical analysis was prespecified for this end point.

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

Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

| End point values                    | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) |  |
|-------------------------------------|---------------------|---------------------|---------------------|--|
| Subject group type                  | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed         | 6                   | 5                   | 8                   |  |
| Units: subjects                     |                     |                     |                     |  |
| Head and Neck: Day 15               | 1                   | 0                   | 0                   |  |
| Respiratory: Day 15                 | 1                   | 0                   | 0                   |  |
| Musculoskeletal/Extremities: Day 22 | 0                   | 1                   | 0                   |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Physical Examinations (Cohort 4)

|                 |  |
|-----------------|--|
| End point title | Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Physical Examinations (Cohort 4) <sup>[6][7]</sup> |
|-----------------|--|

End point description:

At each visit, physical examinations were carried out. Only physical examinations and visits where a clinically significant change from baseline occurred are included below. A clinically significant change from baseline was defined as a change from normal or abnormal (not clinically significant) to abnormal (clinically significant) post-baseline. The complete physical examination included an assessment of general appearance, skin, head and neck (including ears, eyes, nose and throat), lymph nodes, thyroid, musculoskeletal/extremities, abdomen, breast, and cardiovascular, respiratory, neurological, and genital/rectal systems.

The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

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

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No additional statistical analysis was prespecified for this end point.

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

Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

| End point values            | Cohort 4 (25 mg/kg) |  |  |  |
|-----------------------------|---------------------|--|--|--|
| Subject group type          | Reporting group     |  |  |  |
| Number of subjects analysed | 15                  |  |  |  |
| Units: subjects             |                     |  |  |  |
| Abdomen: Day 99             | 1                   |  |  |  |
| General Appearance: Day 211 | 1                   |  |  |  |
| General Appearance: Day 239 | 1                   |  |  |  |
| General Appearance: Day 260 | 1                   |  |  |  |
| General Appearance: Day 281 | 1                   |  |  |  |
| General Appearance: Day 309 | 1                   |  |  |  |
| Genital/Rectal: Day 85      | 1                   |  |  |  |
| Genital/Rectal: Day 99      | 1                   |  |  |  |
| Genital/Rectal: Day 190     | 1                   |  |  |  |
| Genital/Rectal: Day 204     | 1                   |  |  |  |

|                         |   |  |  |  |
|-------------------------|---|--|--|--|
| Genital/Rectal: Day 218 | 1 |  |  |  |
| Genital/Rectal: Day 232 | 1 |  |  |  |
| Genital/Rectal: Day 246 | 1 |  |  |  |
| Genital/Rectal: Day 274 | 1 |  |  |  |
| Genital/Rectal: Day 288 | 1 |  |  |  |
| Genital/Rectal: Day 323 | 1 |  |  |  |
| Head and Neck: Day 78   | 1 |  |  |  |
| Head and Neck: Day 120  | 1 |  |  |  |
| Head and Neck: Day 134  | 1 |  |  |  |
| Head and Neck: Day 148  | 1 |  |  |  |
| Head and Neck: Day 162  | 1 |  |  |  |
| Head and Neck: Day 176  | 1 |  |  |  |
| Head and Neck: Day 190  | 1 |  |  |  |
| Head and Neck: Day 204  | 1 |  |  |  |
| Head and Neck: Day 218  | 1 |  |  |  |
| Head and Neck: Day 232  | 1 |  |  |  |
| Head and Neck: Day 253  | 1 |  |  |  |
| Head and Neck: Day 274  | 1 |  |  |  |
| Head and Neck: Day 302  | 1 |  |  |  |
| Neurological: Day 127   | 1 |  |  |  |
| Neurological: Day 141   | 1 |  |  |  |
| Neurological: Day 155   | 1 |  |  |  |
| Neurological: Day 169   | 1 |  |  |  |
| Neurological: Day 183   | 1 |  |  |  |
| Neurological: Day 197   | 1 |  |  |  |
| Neurological: Day 211   | 1 |  |  |  |
| Neurological: Day 225   | 1 |  |  |  |
| Neurological: Day 239   | 1 |  |  |  |
| Neurological: Day 253   | 1 |  |  |  |
| Neurological: Day 288   | 1 |  |  |  |
| Neurological: Day 309   | 1 |  |  |  |
| Respiratory: Day 50     | 1 |  |  |  |
| Respiratory: Day 85     | 1 |  |  |  |
| Respiratory: Day 127    | 1 |  |  |  |
| Respiratory: Day 141    | 1 |  |  |  |
| Respiratory: Day 155    | 1 |  |  |  |
| Respiratory: Day 169    | 1 |  |  |  |
| Respiratory: Day 183    | 1 |  |  |  |
| Respiratory: Day 197    | 1 |  |  |  |
| Respiratory: Day 211    | 1 |  |  |  |
| Respiratory: Day 225    | 1 |  |  |  |
| Respiratory: Day 239    | 1 |  |  |  |
| Respiratory: Day 253    | 1 |  |  |  |
| Respiratory: Day 288    | 1 |  |  |  |
| Respiratory: Day 309    | 1 |  |  |  |
| Skin: Day 211           | 1 |  |  |  |
| Skin: Day 239           | 1 |  |  |  |
| Skin: Day 260           | 1 |  |  |  |
| Skin: Day 281           | 1 |  |  |  |
| Skin: Day 309           | 1 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Clinical Laboratory Evaluations

|                 |  |
|-----------------|--|
| End point title | Number of Subjects Who Experienced a Clinically Significant Change from Baseline in Clinical Laboratory Evaluations <sup>[8]</sup> |
|-----------------|--|

End point description:

At each visit, routine blood samples were taken for determination of:

- Hematology: hemoglobin, hematocrit, mean corpuscular volume, red blood cell count, platelet count, white blood cell count with differential;
- Blood chemistry: sodium, potassium, calcium, glucose, creatinine, creatinine clearance, blood urea nitrogen, alanine aminotransferase, aspartate aminotransferase, total bilirubin, gamma-glutamyl transferase, C-reactive protein, alkaline phosphatase, lactate dehydrogenase, uric acid, total protein and albumin.

Urinalysis was performed by dipstick method and included: color, clarity/appearance, specific gravity, pH, protein, glucose, ketones, blood, bilirubin, urobilinogen, nitrite, leukocyte esterase, and microscopic examination including red blood cells, white blood cells, cast crystals, and bacteria.

Subjects need to be fasting for at least 8 hours prior to blood glucose assessment. The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

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

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No additional statistical analysis was prespecified for this end point.

| End point values            | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) | Cohort 4 (25 mg/kg) |
|-----------------------------|---------------------|---------------------|---------------------|---------------------|
| Subject group type          | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed | 6                   | 5                   | 8                   | 15                  |
| Units: subjects             | 0                   | 0                   | 3                   | 3                   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Percentage Change from Baseline in Serum Levels of Total Immunoglobulin G (IgG) (Cohorts 1-3)

|                 |   |
|-----------------|---|
| End point title | Mean Percentage Change from Baseline in Serum Levels of Total Immunoglobulin G (IgG) (Cohorts 1-3) <sup>[9]</sup> |
|-----------------|---|

End point description:

Levels of total IgG were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

| End point values                              | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) |  |
|---|---------------------|---------------------|---------------------|--|
| Subject group type                            | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed                   | 3 <sup>[10]</sup>   | 3 <sup>[11]</sup>   | 7 <sup>[12]</sup>   |  |
| Units: percentage change (%)                  |                     |                     |                     |  |
| arithmetic mean (standard error)              |                     |                     |                     |  |
| End of Induction Period (n = 2, 3, 7)         | -55.00 (± 1.400)    | -67.90 (± 3.005)    | -63.44 (± 3.192)    |  |
| End of Maintenance Period (n = 3, 3, 7)       | -4.37 (± 4.834)     | -50.67 (± 3.176)    | -49.21 (± 3.782)    |  |
| End of Treatment-free Follow-up (n = 3, 2, 7) | 23.30 (± 13.141)    | -9.65 (± 21.550)    | -8.54 (± 6.762)     |  |

Notes:

[10] - 'n' in category title denotes number of subjects analyzed for that category.

[11] - 'n' in category title denotes number of subjects analyzed for that category.

[12] - 'n' in category title denotes number of subjects analyzed for that category.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Percentage Change from Baseline in Serum Levels of Total IgG (Cohort 4)

|                 |  |
|-----------------|--|
| End point title | Mean Percentage Change from Baseline in Serum Levels of Total IgG (Cohort 4) <sup>[13]</sup> |
|-----------------|--|

End point description:

Levels of total IgG were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

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

Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

| End point values                 | Cohort 4 (25 mg/kg) |  |  |  |
|----------------------------------|---------------------|--|--|--|
| Subject group type               | Reporting group     |  |  |  |
| Number of subjects analysed      | 15                  |  |  |  |
| Units: percentage change (%)     |                     |  |  |  |
| arithmetic mean (standard error) | -63.53 (± 3.285)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Percentage Change from Baseline in Serum Levels of IgG Subtypes (IgG1, IgG2, IgG3, IgG4) (Cohorts 1-3)

|                 |   |
|-----------------|---|
| End point title | Mean Percentage Change from Baseline in Serum Levels of IgG Subtypes (IgG1, IgG2, IgG3, IgG4) (Cohorts 1-3) <sup>[14]</sup> |
|-----------------|---|

End point description:

Levels of IgG subtypes (IgG1, IgG2, IgG3, IgG4) were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), and the end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)

Notes:

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

Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

| End point values                 | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) |  |
|----------------------------------|---------------------|---------------------|---------------------|--|
| Subject group type               | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed      | 3                   | 3                   | 7                   |  |
| Units: percentage change (%)     |                     |                     |                     |  |
| arithmetic mean (standard error) |                     |                     |                     |  |
| IgG1: End of Induction Period    | -45.83 (± 13.715)   | -69.47 (± 1.785)    | -69.14 (± 3.051)    |  |
| IgG1: End of Maintenance Period  | -7.83 (± 5.210)     | -48.63 (± 1.281)    | -55.67 (± 3.907)    |  |
| IgG2: End of Induction Period    | -45.00 (± 12.501)   | -63.70 (± 5.524)    | -57.11 (± 2.474)    |  |
| IgG2: End of Maintenance Period  | -25.63 (± 6.542)    | -50.17 (± 1.185)    | -49.33 (± 3.729)    |  |
| IgG3: End of Induction Period    | -43.07 (± 16.689)   | -70.30 (± 1.320)    | -65.43 (± 4.153)    |  |
| IgG3: End of Maintenance Period  | -4.37 (± 1.354)     | -45.67 (± 1.955)    | -45.36 (± 5.201)    |  |
| IgG4: End of Induction Period    | -40.43 (± 8.842)    | -61.07 (± 5.374)    | -56.80 (± 5.382)    |  |
| IgG4: End of Maintenance Period  | 7.17 (± 12.856)     | 1.97 (± 58.640)     | -46.94 (± 5.862)    |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Percentage Change from Baseline in Serum Levels of IgG Subtypes (IgG1, IgG2, IgG3, IgG4) (Cohort 4)

|                 |  |
|-----------------|--|
| End point title | Mean Percentage Change from Baseline in Serum Levels of IgG Subtypes (IgG1, IgG2, IgG3, IgG4) (Cohort 4) <sup>[15]</sup> |
|-----------------|--|

End point description:

Levels of IgG subtypes (IgG1, IgG2, IgG3, IgG4) were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

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

Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

| End point values                 | Cohort 4 (25 mg/kg) |  |  |  |
|----------------------------------|---------------------|--|--|--|
| Subject group type               | Reporting group     |  |  |  |
| Number of subjects analysed      | 15                  |  |  |  |
| Units: percentage change (%)     |                     |  |  |  |
| arithmetic mean (standard error) |                     |  |  |  |
| IgG1: End of Induction Period    | -66.95 (± 3.067)    |  |  |  |
| IgG2: End of Induction Period    | -62.54 (± 2.722)    |  |  |  |
| IgG3: End of Induction Period    | -69.15 (± 2.753)    |  |  |  |
| IgG4: End of Induction Period    | -55.85 (± 4.986)    |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-1 Autoantibodies (Cohorts 1-3)

|                 |  |
|-----------------|--|
| End point title | Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-1 Autoantibodies (Cohorts 1-3) <sup>[16]</sup> |
|-----------------|--|

End point description:

Levels of anti-desmoglein-1 were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC. '99999' denotes standard error could not be calculated as only one subject was analyzed.

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

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)



Notes:

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

Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

| End point values                              | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) |  |
|---|---------------------|---------------------|---------------------|--|
| Subject group type                            | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed                   | 1 <sup>[17]</sup>   | 2 <sup>[18]</sup>   | 4 <sup>[19]</sup>   |  |
| Units: percentage change (%)                  |                     |                     |                     |  |
| arithmetic mean (standard error)              |                     |                     |                     |  |
| End of Induction Period (n = 1, 2, 4)         | -64.70 (± 99999)    | 11.85 (± 82.050)    | -50.08 (± 22.920)   |  |
| End of Maintenance Period (n = 1, 1, 4)       | -14.10 (± 99999)    | -88.80 (± 99999)    | -50.23 (± 19.924)   |  |
| End of Treatment-free Follow-up (n = 1, 1, 4) | 25.60 (± 99999)     | -88.20 (± 99999)    | -30.13 (± 51.025)   |  |

Notes:

[17] - 'n' in category title denotes number of subjects analyzed for that category.

[18] - 'n' in category title denotes number of subjects analyzed for that category.

[19] - 'n' in category title denotes number of subjects analyzed for that category.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-1 Autoantibodies (Cohort 4)

|                 |   |
|-----------------|---|
| End point title | Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-1 Autoantibodies (Cohort 4) <sup>[20]</sup> |
|-----------------|---|

End point description:

Levels of anti-desmoglein-1 were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

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

Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

| End point values                 | Cohort 4 (25 mg/kg) |  |  |  |
|----------------------------------|---------------------|--|--|--|
| Subject group type               | Reporting group     |  |  |  |
| Number of subjects analysed      | 13                  |  |  |  |
| Units: percentage change (%)     |                     |  |  |  |
| arithmetic mean (standard error) | -57.81 (± 7.701)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-3 Autoantibodies (Cohorts 1-3)

|                 |  |
|-----------------|--|
| End point title | Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-3 Autoantibodies (Cohorts 1-3) <sup>[21]</sup> |
|-----------------|--|

End point description:

Levels of anti-desmoglein-3 were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), and the end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)

Notes:

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

Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

| End point values                              | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) |  |
|---|---------------------|---------------------|---------------------|--|
| Subject group type                            | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed                   | 3 <sup>[22]</sup>   | 3 <sup>[23]</sup>   | 6 <sup>[24]</sup>   |  |
| Units: percentage change (%)                  |                     |                     |                     |  |
| arithmetic mean (standard error)              |                     |                     |                     |  |
| End of Induction Period (n = 3, 3, 6)         | -20.77 (± 4.100)    | -56.90 (± 12.468)   | -52.63 (± 12.314)   |  |
| End of Maintenance Period (n = 3, 3, 6)       | 72.27 (± 79.268)    | -48.37 (± 19.804)   | -40.62 (± 17.492)   |  |
| End of Treatment-free Follow-up (n = 3, 2, 6) | 213.03 (± 155.219)  | -59.45 (± 25.050)   | -46.52 (± 4.873)    |  |

Notes:

[22] - 'n' in category title denotes number of subjects analyzed for that category.

[23] - 'n' in category title denotes number of subjects analyzed for that category.

[24] - 'n' in category title denotes number of subjects analyzed for that category.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-3 Autoantibodies (Cohort 4)

|                 |   |
|-----------------|---|
| End point title | Mean Percentage Change from Baseline in Serum Levels of Anti-Desmoglein-3 Autoantibodies (Cohort 4) <sup>[25]</sup> |
|-----------------|---|

End point description:

Levels of anti-desmoglein-3 were measured from the blood sampled at Baseline and each visit using a validated assay. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

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

Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

|                                  |                        |  |  |  |
|----------------------------------|------------------------|--|--|--|
| <b>End point values</b>          | Cohort 4 (25 mg/kg)    |  |  |  |
| Subject group type               | Reporting group        |  |  |  |
| Number of subjects analysed      | 10                     |  |  |  |
| Units: percentage change (%)     |                        |  |  |  |
| arithmetic mean (standard error) | -35.32 ( $\pm$ 11.279) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Percentage Change from Baseline in Pemphigus Disease Area Index (PDAI) (Cohorts 1-3)

|                 |   |
|-----------------|---|
| End point title | Mean Percentage Change from Baseline in Pemphigus Disease Area Index (PDAI) (Cohorts 1-3) <sup>[26]</sup> |
|-----------------|---|

End point description:

PDAI is a cutaneous and mucosal disease activity assessment performed by investigator based on evaluation of lesions. The score was weighted for the number and size of lesions with score of 0 (absent) to 10 (> 3 lesions, and/or at least one lesion > 16 cm diameter or entire area) given for skin at 12 anatomic locations, scalp, and mucous membrane showing disease activity (erosions/blisters or new erythema). Damage from post inflammatory hyperpigmentation or erythema from the resolving lesions was scored separately from the main score as absent (0) or present (1) for each body area or scalp resulting in a score of 0 to 12 and 0 to 1. The PDAI total activity score ranged from 0 to 263, with 250 points representing disease activity (120 points for skin activity; 10 points for scalp activity; 120 points for mucosal activity) and 13 points representing disease damage. Higher total activity scores indicate more severe pemphigus symptoms. The Efficacy Analysis Set.

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

End point timeframe:

Baseline (Day 1), end of Induction Period (Day 29), and the end of Maintenance Period (Cohort 1: Day 64; Cohort 2: Day 78; Cohort 3: Day 106), and end of Treatment-free Follow-up (Cohort 1: Day 120; Cohort 2: Day 148; Cohort 3: Day 176)

Notes:

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

Justification: Statistical analysis for Cohort 4 is presented in a separate end point due to the different timeframe.

|   |                        |                        |                        |  |
|---|------------------------|------------------------|------------------------|--|
| <b>End point values</b>                 | Cohort 1 (10 mg/kg)    | Cohort 2 (10 mg/kg)    | Cohort 3 (10 mg/kg)    |  |
| Subject group type                      | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed             | 3 <sup>[27]</sup>      | 3 <sup>[28]</sup>      | 7 <sup>[29]</sup>      |  |
| Units: percentage change (%)            |                        |                        |                        |  |
| arithmetic mean (standard error)        |                        |                        |                        |  |
| End of Induction Period (n = 3, 3, 7)   | -53.77 ( $\pm$ 10.791) | 88.20 ( $\pm$ 161.816) | -58.26 ( $\pm$ 24.617) |  |
| End of Maintenance Period (n = 3, 3, 7) | -23.83 ( $\pm$ 17.629) | -56.20 ( $\pm$ 24.906) | -15.49 ( $\pm$ 69.638) |  |

|   |                 |                  |                   |  |
|---|-----------------|------------------|-------------------|--|
| End of Treatment-free Follow-up (n = 3, 2, 7) | 9.90 (± 46.279) | -76.30 (± 6.300) | -37.86 (± 45.237) |  |
|---|-----------------|------------------|-------------------|--|

Notes:

[27] - 'n' in category title denotes number of subjects analyzed for that category.

[28] - 'n' in category title denotes number of subjects analyzed for that category.

[29] - 'n' in category title denotes number of subjects analyzed for that category.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Percentage Change from Baseline in PDAI (Cohort 4)

|                 |   |
|-----------------|---|
| End point title | Mean Percentage Change from Baseline in PDAI (Cohort 4) <sup>[30]</sup> |
|-----------------|---|

End point description:

PDAI is a cutaneous and mucosal disease activity assessment performed by investigator based on evaluation of lesions. The score was weighted for the number and size of lesions with score of 0 (absent) to 10 (> 3 lesions, and/or at least one lesion > 16 cm diameter or entire area) given for skin at 12 anatomic locations, scalp, and mucous membrane showing disease activity (erosions/blisters or new erythema). Damage from post inflammatory hyperpigmentation or erythema from the resolving lesions was scored separately from the main score as absent (0) or present (1) for each body area or scalp resulting in a score of 0 to 12 and 0 to 1. The PDAI total activity score ranged from 0 to 263, with 250 points representing disease activity (120 points for skin activity; 10 points for scalp activity; 120 points for mucosal activity) and 13 points representing disease damage. Higher total activity scores indicate more severe pemphigus symptoms. The Efficacy Analysis Set.

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

End point timeframe:

Baseline (Day 1) and End of Induction Period (Day 29)

Notes:

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

Justification: Statistical analyses for Cohorts 1-3 are presented in a separate end point due to the different timeframe.

|                                  |                     |  |  |  |
|----------------------------------|---------------------|--|--|--|
| <b>End point values</b>          | Cohort 4 (25 mg/kg) |  |  |  |
| Subject group type               | Reporting group     |  |  |  |
| Number of subjects analysed      | 15                  |  |  |  |
| Units: percentage change (%)     |                     |  |  |  |
| arithmetic mean (standard error) | -55.16 (± 5.474)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Median Time to Disease Control (DC)

|                 |   |
|-----------------|---|
| End point title | Median Time to Disease Control (DC) <sup>[31]</sup> |
|-----------------|---|

End point description:

Time to DC, defined as when new lesions cease to form and established lesions begin to heal, evaluated from visit 2 until control was achieved. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

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

Justification: Statistical analysis for Cohorts 1-3 is pooled using a subject analysis set.

| End point values              | Cohort 4 (25 mg/kg) | Cohorts 1-3          |  |  |
|-------------------------------|---------------------|----------------------|--|--|
| Subject group type            | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed   | 15                  | 16                   |  |  |
| Units: days                   |                     |                      |  |  |
| median (full range (min-max)) | 29 (6 to 64)        | 15 (8 to 92)         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Median Time Until Relapse

|                 |   |
|-----------------|---|
| End point title | Median Time Until Relapse <sup>[32]</sup> |
|-----------------|---|

End point description:

Time until relapse, relapse being defined as the appearance of 3 or more new lesions a month that do not heal spontaneously within 1 week, or as the extension of established lesions, evaluated from any visit after DC. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

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

Justification: Statistical analysis for Cohorts 1-3 is pooled using a subject analysis set.

| End point values              | Cohort 4 (25 mg/kg) | Cohorts 1-3          |  |  |
|-------------------------------|---------------------|----------------------|--|--|
| Subject group type            | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed   | 14 <sup>[33]</sup>  | 14                   |  |  |
| Units: days                   |                     |                      |  |  |
| median (full range (min-max)) | 82 (63 to 211)      | 141 (10 to 169)      |  |  |

Notes:

[33] - Median value represents the lower 95% confidence interval as the median could not be calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Median Time to EoC (Cohort 4)

|                 |   |
|-----------------|---|
| End point title | Median Time to EoC (Cohort 4) <sup>[34]</sup> |
|-----------------|---|

End point description:

Time to EoC was defined as the time at which no new lesions have developed for a minimum of 2 weeks, and approximately 80% of lesions have healed. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

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

Justification: Statistical analysis was prespecified for Cohort 4 only.

| End point values              | Cohort 4 (25 mg/kg) |  |  |  |
|-------------------------------|---------------------|--|--|--|
| Subject group type            | Reporting group     |  |  |  |
| Number of subjects analysed   | 15                  |  |  |  |
| Units: days                   |                     |  |  |  |
| median (full range (min-max)) | 43 (34 to 99)       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Median Time to Complete Clinical Remission (CR) (Cohort 4)

|                 |  |
|-----------------|--|
| End point title | Median Time to Complete Clinical Remission (CR) (Cohort 4) <sup>[35]</sup> |
|-----------------|--|

End point description:

Time to calculated and Investigator-assessed CR, with CR being defined as the absence of new lesions and complete healing of established lesions for Cohort 4. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

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

Justification: Statistical analysis was prespecified for Cohort 4 only.

| End point values              | Cohort 4 (25 mg/kg) |  |  |  |
|-------------------------------|---------------------|--|--|--|
| Subject group type            | Reporting group     |  |  |  |
| Number of subjects analysed   | 15                  |  |  |  |
| Units: days                   |                     |  |  |  |
| median (full range (min-max)) |                     |  |  |  |
| Calculated CR                 | 72 (41 to 287)      |  |  |  |
| Investigator-assessed CR      | 92 (41 to 287)      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Median Time to Complete CR Under Minimal Therapy (Cohort 4)

|                 |   |
|-----------------|---|
| End point title | Median Time to Complete CR Under Minimal Therapy (Cohort 4) <sup>[36]</sup> |
|-----------------|---|

End point description:

CR under minimal therapy was defined as a prednisone dose of 10 mg/day or less for at least 8 weeks. The Efficacy Analysis Set included the population evaluable for efficacy assessment. Subjects evaluable for efficacy were determined by the IDMC.

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

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Notes:

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

Justification: Statistical analysis was prespecified for Cohort 4 only.

| End point values              | Cohort 4 (25 mg/kg) | Cohorts 1-3          |  |  |
|-------------------------------|---------------------|----------------------|--|--|
| Subject group type            | Reporting group     | Subject analysis set |  |  |
| Number of subjects analysed   | 0 <sup>[37]</sup>   | 0 <sup>[38]</sup>    |  |  |
| Units: days                   |                     |                      |  |  |
| median (full range (min-max)) | ( to )              | ( to )               |  |  |

Notes:

[37] - No data was collected for this end point.

[38] - No data was collected for this end point.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Maximum Serum Concentration (Cmax) of Efgartigimod (Cohorts 1-3)

|                 |   |
|-----------------|---|
| End point title | Mean Maximum Serum Concentration (Cmax) of Efgartigimod (Cohorts 1-3) |
|-----------------|---|

End point description:

In order to assess the pharmacokinetic (PK) parameters of efgartigimod, blood samples were collected from each subject at each visit from Baseline. Concentrations of serum efgartigimod were determined using a validated assay. The PK Analysis Set included all subjects in the SAS who have at least one evaluable time-point of efgartigimod PK concentration data. No PK parameters were derived from Cohort 4.

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

End point timeframe:

Within 30 minutes prior to start of infusion for the predose sample and within 30 minutes after end of infusion for the postdose sample at Baseline (Day 1) and Days 8, 15, 22, 36, 50, 64, 78, 92, and 106

| End point values                     | Cohorts 1-3          |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 19 <sup>[39]</sup>   |  |  |  |
| Units: micrograms (µg)/mL            |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Day 1 (n = 19)                       | 168.748 (± 74.4491)  |  |  |  |
| Day 8 (n = 19)                       | 171.079 (± 51.0213)  |  |  |  |
| Day 15 (n = 17)                      | 147.829 (± 55.9076)  |  |  |  |
| Day 22 (n = 15)                      | 209.147 (± 212.4485) |  |  |  |
| Day 36 (n = 11)                      | 173.209 (± 49.3980)  |  |  |  |
| Day 50 (n = 10)                      | 164.590 (± 59.4498)  |  |  |  |
| Day 64 (n = 12)                      | 229.333 (± 251.7157) |  |  |  |
| Day 78 (n = 10)                      | 227.100 (± 189.2784) |  |  |  |
| Day 92 (n = 7)                       | 195.286 (± 73.6698)  |  |  |  |
| Day 106 (n = 7)                      | 168.071 (± 80.1428)  |  |  |  |

Notes:

[39] - 'n' in category title denotes number of subjects analyzed for that category.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Median Time to Cmax (Tmax) of Efgartigimod (Cohorts 1-3)

|                 |  |
|-----------------|--|
| End point title | Median Time to Cmax (Tmax) of Efgartigimod (Cohorts 1-3) |
|-----------------|--|

End point description:

In order to assess the PK parameters of efgartigimod, blood samples were collected from each subject at each visit from Baseline. Concentrations of serum efgartigimod were determined using a validated assay. The PK Analysis Set included all subjects in the SAS who have at least one evaluable time-point of efgartigimod PK concentration data. No PK parameters were derived from Cohort 4.

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

End point timeframe:

Within 30 minutes prior to start of infusion for the predose sample and within 30 minutes after end of infusion for the postdose sample at Baseline (Day 1) and Days 8, 15, 22, 36, 50, 64, 78, 92, and 106

| End point values              | Cohorts 1-3          |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 19 <sup>[40]</sup>   |  |  |  |
| Units: hours (h)              |                      |  |  |  |
| median (full range (min-max)) |                      |  |  |  |
| Day 1 (n = 19)                | 2.500 (2.50 to 2.50) |  |  |  |
| Day 8 (n = 19)                | 2.317 (2.03 to 2.55) |  |  |  |



|                 |                      |  |  |  |
|-----------------|----------------------|--|--|--|
| Day 15 (n = 17) | 2.250 (2.03 to 2.50) |  |  |  |
| Day 22 (n = 15) | 2.300 (2.13 to 2.50) |  |  |  |
| Day 36 (n = 11) | 2.250 (2.05 to 2.50) |  |  |  |
| Day 50 (n = 10) | 2.267 (2.08 to 2.50) |  |  |  |
| Day 64 (n = 12) | 2.450 (2.08 to 3.33) |  |  |  |
| Day 78 (n = 10) | 2.425 (2.08 to 2.50) |  |  |  |
| Day 92 (n = 7)  | 2.333 (2.08 to 2.50) |  |  |  |
| Day 106 (n = 7) | 2.283 (2.08 to 2.50) |  |  |  |

Notes:

[40] - 'n' in category title denotes number of subjects analyzed for that category.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Concentration of Efgartigimod at the End of the Dosing Interval (Ctough) (Cohorts 1-3)

|                 |   |
|-----------------|---|
| End point title | Mean Concentration of Efgartigimod at the End of the Dosing Interval (Ctough) (Cohorts 1-3) |
|-----------------|---|

End point description:

In order to assess the PK parameters of efgartigimod, blood samples were collected from each subject at each visit from Baseline. Concentrations of serum efgartigimod were determined using a validated assay. The PK Analysis Set included all subjects in the SAS who have at least one evaluable time-point of efgartigimod PK concentration data. No PK parameters were derived from Cohort 4.

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

End point timeframe:

Within 30 minutes prior to start of infusion for the predose sample and within 30 minutes after end of infusion for the postdose sample on Days 8, 15, 22, 36, 50, 64, 78, 92, and 106

| End point values                     | Cohorts 1-3          |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 19 <sup>[41]</sup>   |  |  |  |
| Units: µg/mL                         |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Day 8 (n = 19)                       | 9.395 (± 5.2388)     |  |  |  |
| Day 15 (n = 18)                      | 10.742 (± 5.9878)    |  |  |  |
| Day 22 (n = 15)                      | 11.164 (± 7.5341)    |  |  |  |
| Day 29 (n = 14)                      | 12.993 (± 6.5653)    |  |  |  |
| Day 36 (n = 12)                      | 3.519 (± 2.3757)     |  |  |  |
| Day 50 (n = 10)                      | 3.044 (± 2.1179)     |  |  |  |

|                 |                  |  |  |  |
|-----------------|------------------|--|--|--|
| Day 64 (n = 12) | 1.883 (± 1.8393) |  |  |  |
| Day 78 (n = 10) | 3.257 (± 1.9766) |  |  |  |
| Day 92 (n = 7)  | 2.581 (± 1.2742) |  |  |  |
| Day 106 (n = 7) | 2.469 (± 1.5568) |  |  |  |

Notes:

[41] - 'n' in category title denotes number of subjects analyzed for that category.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Experiencing Postdose Antidrug Antibodies (ADA) to Efgartigimod

|                 |  |
|-----------------|--|
| End point title | Number of Subjects Experiencing Postdose Antidrug Antibodies (ADA) to Efgartigimod |
|-----------------|--|

End point description:

In Cohorts 1-3, blood samples to assess ADA were collected at Baseline, Visit 3, Visit 5, all Maintenance treatment visits, Follow-up 1, Follow-up 2 and Follow-up 3. In Cohort 4, blood samples to assess ADA were collected at Baseline, then biweekly until End of Treatment, and at each Follow-up visit. The Full Analysis Set included all subjects who received at least one dose of study drug.

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

End point timeframe:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

|                             |                      |  |  |  |
|-----------------------------|----------------------|--|--|--|
| <b>End point values</b>     | Cohorts 1-4          |  |  |  |
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 31                   |  |  |  |
| Units: subjects             | 3                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the start of the first IMP (Day 1) up to end of the follow-up period, approximately 44 weeks

Adverse event reporting additional description:

The SAS included all enrolled subjects who received at least 1 dose of efgartigimod.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Cohort 1 (10 mg/kg) |
|-----------------------|---------------------|

Reporting group description:

Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period at weeks 2 and 6.

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Cohort 2 (10 mg/kg) |
|-----------------------|---------------------|

Reporting group description:

Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period once q2w for 8 weeks.

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Cohort 3 (10 mg/kg) |
|-----------------------|---------------------|

Reporting group description:

Efgartigimod IV 10 mg/kg was administered as 4 weekly infusions during the induction period and during the maintenance period q2w for 12 weeks.

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Cohort 4 (25 mg/kg) |
|-----------------------|---------------------|

Reporting group description:

Efgartigimod IV 25 mg/kg was administered as 5 weekly infusions (minimum) during the induction period until EoC, and during the maintenance period q2w until Week 34.

| Serious adverse events                            | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) |
|---|---------------------|---------------------|---------------------|
| Total subjects affected by serious adverse events |                     |                     |                     |
| subjects affected / exposed                       | 1 / 6 (16.67%)      | 1 / 5 (20.00%)      | 0 / 8 (0.00%)       |
| number of deaths (all causes)                     | 0                   | 0                   | 0                   |
| number of deaths resulting from adverse events    | 0                   | 0                   | 0                   |
| Injury, poisoning and procedural complications    |                     |                     |                     |
| Tibia fracture                                    |                     |                     |                     |
| subjects affected / exposed                       | 0 / 6 (0.00%)       | 1 / 5 (20.00%)      | 0 / 8 (0.00%)       |
| occurrences causally related to treatment / all   | 0 / 0               | 0 / 1               | 0 / 0               |
| deaths causally related to treatment / all        | 0 / 0               | 0 / 0               | 0 / 0               |
| Infections and infestations                       |                     |                     |                     |
| Pneumonia   |                     |                     |                     |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |

|   |                     |  |  |
|---|---------------------|--|--|
| <b>Serious adverse events</b>                     | Cohort 4 (25 mg/kg) |  |  |
| Total subjects affected by serious adverse events |                     |  |  |
| subjects affected / exposed                       | 0 / 15 (0.00%)      |  |  |
| number of deaths (all causes)                     | 0                   |  |  |
| number of deaths resulting from adverse events    | 0                   |  |  |
| Injury, poisoning and procedural complications    |                     |  |  |
| Tibia fracture                                    |                     |  |  |
| subjects affected / exposed                       | 0 / 15 (0.00%)      |  |  |
| occurrences causally related to treatment / all   | 0 / 0               |  |  |
| deaths causally related to treatment / all        | 0 / 0               |  |  |
| Infections and infestations                       |                     |  |  |
| Pneumonia   |                     |  |  |
| subjects affected / exposed                       | 0 / 15 (0.00%)      |  |  |
| occurrences causally related to treatment / all   | 0 / 0               |  |  |
| deaths causally related to treatment / all        | 0 / 0               |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| <b>Non-serious adverse events</b>                     | Cohort 1 (10 mg/kg) | Cohort 2 (10 mg/kg) | Cohort 3 (10 mg/kg) |
| Total subjects affected by non-serious adverse events |                     |                     |                     |
| subjects affected / exposed                           | 6 / 6 (100.00%)     | 3 / 5 (60.00%)      | 6 / 8 (75.00%)      |
| Vascular disorders                                    |                     |                     |                     |
| Flushing  |                     |                     |                     |
| subjects affected / exposed                           | 0 / 6 (0.00%)       | 0 / 5 (0.00%)       | 0 / 8 (0.00%)       |
| occurrences (all)                                     | 0                   | 0                   | 0                   |
| Hypertension  |                     |                     |                     |
| subjects affected / exposed                           | 0 / 6 (0.00%)       | 0 / 5 (0.00%)       | 0 / 8 (0.00%)       |
| occurrences (all)                                     | 0                   | 0                   | 0                   |
| General disorders and administration site conditions  |                     |                     |                     |
| Fatigue   |                     |                     |                     |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 2              | 0              | 0              |
| Influenza like illness                          |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 2              |
| Pyrexia   |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 3              | 0              | 0              |
| Infusion site swelling                          |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Hernia pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Oedema peripheral                               |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Oropharyngeal pain                              |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 2              |
| Nasal dryness                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Cough   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                               | 0              | 0              | 2              |
| Respiratory failure                             |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Psychiatric disorders                           |                |                |                |
| Anxiety   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Investigations                                  |                |                |                |

|   |                     |                    |                     |
|---|---------------------|--------------------|---------------------|
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Cystatin C increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Injury, poisoning and procedural complications<br>Traumatic ulcer<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Cardiac disorders<br>Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 6 (16.67%)<br>3 | 0 / 5 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Headache<br>subjects affected / exposed<br>occurrences (all)  | 1 / 6 (16.67%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Paraesthesia  |                     |                    |                     |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                 | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Syncope<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 6 (16.67%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Blood and lymphatic system disorders   |                     |                    |                     |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Neutrophilia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Anaemia macrocytic<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Ear and labyrinth disorders  |                     |                    |                     |
| Excessive cerumen production<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Middle ear inflammation<br>subjects affected / exposed<br>occurrences (all)      | 1 / 6 (16.67%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Eye disorders  |                     |                    |                     |
| Blindness transient<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Gastrointestinal disorders   |                     |                    |                     |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 2 / 8 (25.00%)<br>2 |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)               | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 6 (16.67%)<br>1 | 0 / 5 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Dyspepsia  |                     |                    |                     |

|  |                |               |                |
|--|----------------|---------------|----------------|
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 1              | 0             | 0              |
| Abdominal pain upper                   |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Nausea                                 |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Gastrointestinal disorder              |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)                      | 0              | 0             | 1              |
| Oral pain                              |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Toothache                              |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Oral disorder                          |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Skin and subcutaneous tissue disorders |                |               |                |
| Dry skin                               |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all)                      | 0              | 0             | 1              |
| Alopecia                               |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Psoriasis                              |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Pruritus                               |                |               |                |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 1              | 0             | 0              |
| Rash erythematous                      |                |               |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 5 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |



|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| Urticaria<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Renal and urinary disorders<br>Renal cyst<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 6 (16.67%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Renal pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 6 (16.67%)<br>2 | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Endocrine disorders<br>Cushingoid<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1 | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 | 0 / 8 (0.00%)<br>0  |
| Muscular weakness<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  | 1 / 8 (12.50%)<br>2 |
| Rhinitis  |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Bronchitis                  |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 1              | 0              | 1              |
| Gastroenteritis             |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Impetigo                    |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Pustule                     |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0              | 2              |
| Bacteriuria                 |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)           | 0              | 0              | 1              |
| Candida infection           |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Oral herpes                 |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Conjunctivitis              |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 5 (20.00%) | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Folliculitis                |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pulpitis dental             |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Respiratory tract infection |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 5 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Sialoadenitis               |                |                |                |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Tonsillitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 6 (16.67%)<br>1 | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Skin infection<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Type 2 diabetes mellitus<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |

|   |                      |  |  |
|---|----------------------|--|--|
| <b>Non-serious adverse events</b>   | Cohort 4 (25 mg/kg)  |  |  |
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed                                | 13 / 15 (86.67%)     |  |  |
| Vascular disorders<br>Flushing<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 15 (6.67%)<br>1  |  |  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1  |  |  |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1  |  |  |
| Influenza like illness<br>subjects affected / exposed<br>occurrences (all)  | 2 / 15 (13.33%)<br>4 |  |  |
| Pyrexia   |                      |  |  |

|   |  |  |  |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>0 / 15 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>  |  |  |  |
| <p>Infusion site swelling</p> <p>subjects affected / exposed</p> <p>0 / 15 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>  |  |  |  |
| <p>Hernia pain</p> <p>subjects affected / exposed</p> <p>0 / 15 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |
| <p>Oedema peripheral</p> <p>subjects affected / exposed</p> <p>0 / 15 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Oropharyngeal pain</p> <p>subjects affected / exposed</p> <p>0 / 15 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Nasal dryness</p> <p>subjects affected / exposed</p> <p>0 / 15 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>1 / 15 (6.67%)</p> <p>occurrences (all)</p> <p>1</p> <p>Respiratory failure</p> <p>subjects affected / exposed</p> <p>0 / 15 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> |  |  |  |
| <p>Psychiatric disorders</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>1 / 15 (6.67%)</p> <p>occurrences (all)</p> <p>1</p>  |  |  |  |
| <p>Investigations</p> <p>Alanine aminotransferase increased</p> <p>subjects affected / exposed</p> <p>2 / 15 (13.33%)</p> <p>occurrences (all)</p> <p>2</p> <p>Aspartate aminotransferase increased</p> <p>subjects affected / exposed</p> <p>1 / 15 (6.67%)</p> <p>occurrences (all)</p> <p>1</p> <p>Blood creatine phosphokinase</p>  |  |  |  |

|  |   |  |  |
|--|---|--|--|
| increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1   |  |  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1   |  |  |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1   |  |  |
| Cystatin C increased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1   |  |  |
| Injury, poisoning and procedural complications<br>Traumatic ulcer<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1   |  |  |
| Cardiac disorders<br>Tachycardia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0   |  |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Paraesthesia<br>subjects affected / exposed<br>occurrences (all)<br><br>Syncope<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1<br><br>3 / 15 (20.00%)<br>3<br><br>1 / 15 (6.67%)<br>1<br><br>0 / 15 (0.00%)<br>0 |  |  |
| Blood and lymphatic system disorders<br>Anaemia  |   |  |  |

|                              |                 |  |  |
|------------------------------|-----------------|--|--|
| subjects affected / exposed  | 2 / 15 (13.33%) |  |  |
| occurrences (all)            | 2               |  |  |
| Neutrophilia                 |                 |  |  |
| subjects affected / exposed  | 0 / 15 (0.00%)  |  |  |
| occurrences (all)            | 0               |  |  |
| Anaemia macrocytic           |                 |  |  |
| subjects affected / exposed  | 0 / 15 (0.00%)  |  |  |
| occurrences (all)            | 0               |  |  |
| Ear and labyrinth disorders  |                 |  |  |
| Excessive cerumen production |                 |  |  |
| subjects affected / exposed  | 0 / 15 (0.00%)  |  |  |
| occurrences (all)            | 0               |  |  |
| Middle ear inflammation      |                 |  |  |
| subjects affected / exposed  | 0 / 15 (0.00%)  |  |  |
| occurrences (all)            | 0               |  |  |
| Eye disorders                |                 |  |  |
| Blindness transient          |                 |  |  |
| subjects affected / exposed  | 1 / 15 (6.67%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Gastrointestinal disorders   |                 |  |  |
| Diarrhoea                    |                 |  |  |
| subjects affected / exposed  | 2 / 15 (13.33%) |  |  |
| occurrences (all)            | 3               |  |  |
| Abdominal pain               |                 |  |  |
| subjects affected / exposed  | 2 / 15 (13.33%) |  |  |
| occurrences (all)            | 2               |  |  |
| Vomiting                     |                 |  |  |
| subjects affected / exposed  | 1 / 15 (6.67%)  |  |  |
| occurrences (all)            | 1               |  |  |
| Dyspepsia                    |                 |  |  |
| subjects affected / exposed  | 0 / 15 (0.00%)  |  |  |
| occurrences (all)            | 0               |  |  |
| Abdominal pain upper         |                 |  |  |
| subjects affected / exposed  | 1 / 15 (6.67%)  |  |  |
| occurrences (all)            | 2               |  |  |
| Nausea                       |                 |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed            | 1 / 15 (6.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Gastrointestinal disorder              |                |  |  |
| subjects affected / exposed            | 0 / 15 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Oral pain                              |                |  |  |
| subjects affected / exposed            | 1 / 15 (6.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Toothache                              |                |  |  |
| subjects affected / exposed            | 1 / 15 (6.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Oral disorder                          |                |  |  |
| subjects affected / exposed            | 1 / 15 (6.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Skin and subcutaneous tissue disorders |                |  |  |
| Dry skin                               |                |  |  |
| subjects affected / exposed            | 1 / 15 (6.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Alopecia                               |                |  |  |
| subjects affected / exposed            | 1 / 15 (6.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Psoriasis                              |                |  |  |
| subjects affected / exposed            | 1 / 15 (6.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Pruritus                               |                |  |  |
| subjects affected / exposed            | 0 / 15 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Rash erythematous                      |                |  |  |
| subjects affected / exposed            | 1 / 15 (6.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Urticaria                              |                |  |  |
| subjects affected / exposed            | 0 / 15 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Renal and urinary disorders            |                |  |  |
| Renal cyst                             |                |  |  |

|  |   |  |  |
|--|---|--|--|
| subjects affected / exposed<br>occurrences (all)<br><br>Renal pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0<br><br>1 / 15 (6.67%)<br>1  |  |  |
| Endocrine disorders<br>Cushingoid<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1   |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Back pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Muscular weakness<br>subjects affected / exposed<br>occurrences (all)<br><br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)       | 0 / 15 (0.00%)<br>0<br><br>0 / 15 (0.00%)<br>0<br><br>1 / 15 (6.67%)<br>1<br><br>0 / 15 (0.00%)<br>0    |  |  |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)<br><br>Rhinitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Gastroenteritis | 4 / 15 (26.67%)<br>4<br><br>2 / 15 (13.33%)<br>2<br><br>2 / 15 (13.33%)<br>3<br><br>0 / 15 (0.00%)<br>0 |  |  |



|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 15 (6.67%) |  |  |
| occurrences (all)           | 1              |  |  |
| Impetigo                    |                |  |  |
| subjects affected / exposed | 1 / 15 (6.67%) |  |  |
| occurrences (all)           | 1              |  |  |
| Pustule                     |                |  |  |
| subjects affected / exposed | 0 / 15 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Bacteriuria                 |                |  |  |
| subjects affected / exposed | 0 / 15 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Candida infection           |                |  |  |
| subjects affected / exposed | 1 / 15 (6.67%) |  |  |
| occurrences (all)           | 1              |  |  |
| Oral herpes                 |                |  |  |
| subjects affected / exposed | 0 / 15 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Conjunctivitis              |                |  |  |
| subjects affected / exposed | 0 / 15 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Folliculitis                |                |  |  |
| subjects affected / exposed | 1 / 15 (6.67%) |  |  |
| occurrences (all)           | 1              |  |  |
| Pulpitis dental             |                |  |  |
| subjects affected / exposed | 1 / 15 (6.67%) |  |  |
| occurrences (all)           | 1              |  |  |
| Respiratory tract infection |                |  |  |
| subjects affected / exposed | 0 / 15 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Sialoadenitis               |                |  |  |
| subjects affected / exposed | 0 / 15 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Tonsillitis                 |                |  |  |
| subjects affected / exposed | 0 / 15 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Skin infection              |                |  |  |

|                                    |                |  |  |
|------------------------------------|----------------|--|--|
| subjects affected / exposed        | 1 / 15 (6.67%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Tooth infection                    |                |  |  |
| subjects affected / exposed        | 1 / 15 (6.67%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Upper respiratory tract infection  |                |  |  |
| subjects affected / exposed        | 1 / 15 (6.67%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Metabolism and nutrition disorders |                |  |  |
| Type 2 diabetes mellitus           |                |  |  |
| subjects affected / exposed        | 0 / 15 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 20 October 2017  | The following sections of the protocol were updated: <ul style="list-style-type: none"><li>- Schedule of Assessments</li><li>- Section 5.1 Summary of Study Design</li><li>- Section 5.3 Selection of Study Population</li><li>- Section 5.3.1 Inclusion Criteria</li><li>- Section 5.3.2 Exclusion Criteria</li><li>- Section 6.3.4 Visit 6 and Visit 7 (Maintenance treatment period)</li><li>- Section 6.6 Unscheduled Visit</li><li>- Section 8.1.2.2 Other Laboratory Assessments</li><li>- Section 9.2 Quality Control of Data</li><li>- Section 10.2 Statistical Methods</li></ul>   |
| 28 February 2018 | The following sections of the protocol were updated: <ul style="list-style-type: none"><li>- Section 3.1 Primary Objectives</li><li>- Section 5.3 Selection of Study Population</li><li>- Synopsis Section 5.3.1 Inclusion Criteria</li><li>- Synopsis Methodology</li><li>- Section 11.4 Patient Data Protection</li></ul>   |
| 11 June 2018     | The following sections of the protocol were updated: <ul style="list-style-type: none"><li>- Section 5.1 Summary of Study Design</li><li>- Schedule of Assessments</li><li>- Section 5.3.1 Inclusion Criteria</li><li>- Section 5.3.6 Sample Size Increase</li><li>- Section 7.7 Prior and Concomitant Treatments</li><li>- Section 7.8.1 Rescue Therapy</li><li>- Section 8.1.2.2 Other Laboratory Assessments</li></ul>   |
| 06 February 2019 | The following sections of the protocol were updated: <ul style="list-style-type: none"><li>- Section 3 Study Objectives</li><li>- Section 4.2 Secondary endpoints</li><li>- Section 5.1 Summary of Study Design</li><li>- Section 5.3.6 Sample Size Increase</li><li>- Section 5.3.1 Inclusion Criteria</li><li>- Section 5.3.8 Screen Failures and Rescreening</li><li>- Section 6.2 Screening</li><li>- Sections 6.4, 6.5.1, 8.1.2.2 Assessments</li><li>- Section 7.1 Treatments Administered</li><li>- Section 7.7 Prior and Concomitant Treatments</li><li>- Section 7.8.1 Rescue Therapy</li><li>- Section 8.1.2.2 Other Laboratory Assessments</li><li>- Section 8.5 Antidrug Antibodies</li><li>- Section 10.4 Interim Analysis</li></ul> |
| 26 June 2019     | The following sections of the protocol were updated: <ul style="list-style-type: none"><li>- Section 6.4.2 Visit 2 to EoC</li><li>- Section 7.1 Treatments Administered</li></ul>   |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported