



## Clinical trial results:

**A European, randomised, double-blind, active comparator-controlled, cross-over, efficacy and safety study of a new 10% ready-to-use liquid human intravenous immunoglobulin (I10E) versus Kiovig® in patients with Multifocal Motor Neuropathy .**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-001995-12 |
| Trial protocol           | IT GB ES FR    |
| Global end of trial date | 01 July 2016   |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 03 June 2017 |
| First version publication date | 03 June 2017 |

### Trial information

#### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | I10E-0901 |
|-----------------------|-----------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |                                                                            |
|------------------------------|----------------------------------------------------------------------------|
| Sponsor organisation name    | LFB Biotechnologies                                                        |
| Sponsor organisation address | 3, Avenue des Tropiques - BP 40305, COURTABOEUF, France, 91958             |
| Public contact               | Global Clinical Development Leader, LFB BIOTECHNOLOGIES, +33 169 82 56 56, |
| Scientific contact           | Global Clinical Development Leader, LFB BIOTECHNOLOGIES, +33 169 82 56 56, |

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                       | 04 November 2016 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 01 July 2016     |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 01 July 2016     |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of I10E compared to Kiovig® for maintenance treatment of patients with MMN in a randomised, double-blind, active comparator-controlled, cross-over design.

Protection of trial subjects:

No specific protection.

Background therapy:

None

Evidence for comparator:

The comparator was Kiovig, the only human normal immunoglobulin with an indication in Multifocal Motor Neuropathy when the study protocol was written

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 04 September 2013 |
| 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 | Spain: 6          |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | France: 6         |
| Country: Number of subjects enrolled | Italy: 9          |
| Worldwide total number of subjects   | 23                |
| EEA total number of subjects         | 23                |

Notes:

### Subjects enrolled per age group

|                                           |   |
|-------------------------------------------|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |
| Children (2-11 years)                     | 0 |
| Adolescents (12-17 years)                 | 0 |

|                      |    |
|----------------------|----|
| Adults (18-64 years) | 22 |
| From 65 to 84 years  | 1  |
| 85 years and over    | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The first patient signed a consent form on 4 September 2013

The last patient signed a consent form on 2 July 2015

### Pre-assignment

Screening details:

A blood sample was drawn during the screening visit for laboratory tests, in order to rule out some exclusion criteria.

### Pre-assignment period milestones

|                            |                   |
|----------------------------|-------------------|
| Number of subjects started | 30 <sup>[1]</sup> |
|----------------------------|-------------------|

|                              |    |
|------------------------------|----|
| Number of subjects completed | 22 |
|------------------------------|----|

### Pre-assignment subject non-completion reasons

|                            |                      |
|----------------------------|----------------------|
| Reason: Number of subjects | screening failure: 8 |
|----------------------------|----------------------|

Notes:

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

Justification: 8 patients are on screening failure.

### Period 1

|                |                                         |
|----------------|-----------------------------------------|
| Period 1 title | Before 1st administration of study drug |
|----------------|-----------------------------------------|

|                              |     |
|------------------------------|-----|
| Is this the baseline period? | Yes |
|------------------------------|-----|

|                   |                         |
|-------------------|-------------------------|
| Allocation method | Randomised - controlled |
|-------------------|-------------------------|

|               |              |
|---------------|--------------|
| Blinding used | Double blind |
|---------------|--------------|

|               |                                                               |
|---------------|---------------------------------------------------------------|
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |
|---------------|---------------------------------------------------------------|

Blinding implementation details:

Before shipment to investigational sites, each vial of IMP was covered by a masking system and was packaged in an individual box. Each vial and box was labelled with a unique identification number and all other useful information for the study except information enabling the identification of IMP. Before each course, the hospital pharmacist logged in the IWRS and obtained the vial identification numbers for vials to be administered to the subject.

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|           |                |
|-----------|----------------|
| Arm title | Sequence A arm |
|-----------|----------------|

Arm description:

The patients randomized in Sequence A received Kiovig in Period 1 and I10E in period 2.

|          |                   |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

|                                        |        |
|----------------------------------------|--------|
| Investigational medicinal product name | Kiovig |
|----------------------------------------|--------|

|                                        |  |
|----------------------------------------|--|
| Investigational medicinal product code |  |
|----------------------------------------|--|

|            |  |
|------------|--|
| Other name |  |
|------------|--|

|                      |                       |
|----------------------|-----------------------|
| Pharmaceutical forms | Solution for infusion |
|----------------------|-----------------------|

|                          |                 |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

No administration during this period.

|           |                |
|-----------|----------------|
| Arm title | Sequence B arm |
|-----------|----------------|

Arm description:

The patients randomized in Sequence B received I10E in Period 1 and Kiovig in period 2.

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

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | I10E                  |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

No administration during this period.

| <b>Number of subjects in period 1<sup>[2]</sup></b> | Sequence A arm | Sequence B arm |
|-----------------------------------------------------|----------------|----------------|
| Started                                             | 12             | 10             |
| Completed                                           | 12             | 10             |

Notes:

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

Justification: 23 patients randomized (worldwide number) but one patient on screening failure after randomization.

## Period 2

|                              |                                                               |
|------------------------------|---------------------------------------------------------------|
| Period 2 title               | Treatment period 1                                            |
| Is this the baseline period? | No                                                            |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind                                                  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Blinding implementation details:

Before shipment to investigational sites, each vial of IMP was covered by a masking system and was packaged in an individual box. Each vial and box was labelled with a unique identification number and all other useful information for the study except information enabling the identification of IMP. Before each course, the hospital pharmacist logged in the IWRS and obtained the vial identification numbers for vials to be administered to the subject.

## Arms

|                              |                |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes            |
| <b>Arm title</b>             | Sequence A arm |

Arm description:

The patients randomized in Sequence A received Kiovig in Period 1 and I10E in period 2.

|                                        |                       |
|----------------------------------------|-----------------------|
| Arm type                               | Active comparator     |
| Investigational medicinal product name | Kiovig                |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

Dosage and treatment course frequency could vary from subject to subject. The treatment schedule was to be maintained stable at the same level as before inclusion into the study. The allowed range was between 1 g/kg over 1-3 days and 2 g/kg over 2-5 days every 4 to 8 weeks.

I10E and Kiovig were administered in a double-blind manner by investigators.

Duration of treatment:

Randomized subjects were treated for between 42 and 50 weeks including two 21 to 25-week periods with Kiovig and I10E or vice versa. The exact duration of the treatment and follow-up depended on each subject's own schedule.

|                                                                                                             |                       |
|-------------------------------------------------------------------------------------------------------------|-----------------------|
| <b>Arm title</b>                                                                                            | sequence B arm        |
| Arm description:<br>The patients randomized in Sequence B received I10E in Period 1 and Kiovig in period 2. |                       |
| Arm type                                                                                                    | Experimental          |
| Investigational medicinal product name                                                                      | I10E                  |
| Investigational medicinal product code                                                                      |                       |
| Other name                                                                                                  |                       |
| Pharmaceutical forms                                                                                        | Solution for infusion |
| Routes of administration                                                                                    | Intravenous use       |

**Dosage and administration details:**

Dosage and treatment course frequency could vary from subject to subject. The treatment schedule was to be maintained stable at the same level as before inclusion into the study. The allowed range was between 1 g/kg over 1-3 days and 2 g/kg over 2-5 days every 4 to 8 weeks.

I10E and Kiovig were administered in a double-blind manner by investigators.

**Duration of treatment:**

Randomized subjects were treated for between 42 and 50 weeks including two 21 to 25-week periods with Kiovig and I10E or vice versa. The exact duration of the treatment and follow-up depended on each subject's own schedule.

| <b>Number of subjects in period 2</b> | Sequence A arm | sequence B arm |
|---------------------------------------|----------------|----------------|
| Started                               | 12             | 10             |
| Completed                             | 12             | 9              |
| Not completed                         | 0              | 1              |
| Patient dissatisfaction with IMP      | -              | 1              |

**Period 3**

|                              |                                                               |
|------------------------------|---------------------------------------------------------------|
| Period 3 title               | Treatment period 2                                            |
| Is this the baseline period? | No                                                            |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind                                                  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

**Blinding implementation details:**

Before shipment to investigational sites, each vial of IMP was covered by a masking system and was packaged in an individual box. Each vial and box was labelled with a unique identification number and all other useful information for the study except information enabling the identification of IMP. Before each course, the hospital pharmacist logged in the IWRS and obtained the vial identification numbers for vials to be administered to the subject.

**Arms**

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                                                                                          |                       |
|------------------------------------------------------------------------------------------|-----------------------|
| <b>Arm title</b>                                                                         | Sequence A arm        |
| Arm description:<br>The patients randomized in Sequence A received I10E during Period 2. |                       |
| Arm type                                                                                 | Experimental          |
| Investigational medicinal product name                                                   | I10E                  |
| Investigational medicinal product code                                                   |                       |
| Other name                                                                               |                       |
| Pharmaceutical forms                                                                     | Solution for infusion |
| Routes of administration                                                                 | Intravenous use       |

**Dosage and administration details:**

Dosage and treatment course frequency could vary from subject to subject. The treatment schedule was to be maintained stable at the same level as before inclusion into the study. The allowed range was between 1 g/kg over 1-3 days and 2 g/kg over 2-5 days every 4 to 8 weeks.

I10E and Kiovig were administered in a double-blind manner by investigators.

**Duration of treatment:**

Randomized subjects were treated for between 42 and 50 weeks including two 21 to 25-week periods with Kiovig and I10E or vice versa. The exact duration of the treatment and follow-up depended on each subject's own schedule.

|                                                                                            |                       |
|--------------------------------------------------------------------------------------------|-----------------------|
| <b>Arm title</b>                                                                           | Sequence B arm        |
| Arm description:<br>The patients randomized in Sequence B received Kiovig during period 2. |                       |
| Arm type                                                                                   | Active comparator     |
| Investigational medicinal product name                                                     | Kiovig                |
| Investigational medicinal product code                                                     |                       |
| Other name                                                                                 |                       |
| Pharmaceutical forms                                                                       | Solution for infusion |
| Routes of administration                                                                   | Intravenous use       |

**Dosage and administration details:**

Dosage and treatment course frequency could vary from subject to subject. The treatment schedule was to be maintained stable at the same level as before inclusion into the study. The allowed range was between 1 g/kg over 1-3 days and 2 g/kg over 2-5 days every 4 to 8 weeks.

I10E and Kiovig were administered in a double-blind manner by investigators.

**Duration of treatment:**

Randomized subjects were treated for between 42 and 50 weeks including two 21 to 25-week periods with Kiovig and I10E or vice versa. The exact duration of the treatment and follow-up depended on each subject's own schedule.

| <b>Number of subjects in period 3</b> | Sequence A arm | Sequence B arm |
|---------------------------------------|----------------|----------------|
| Started                               | 12             | 9              |
| Completed                             | 12             | 9              |

## Baseline characteristics

### Reporting groups

|                                                                                                                         |                |
|-------------------------------------------------------------------------------------------------------------------------|----------------|
| Reporting group title                                                                                                   | Sequence A arm |
| Reporting group description:<br>The patients randomized in Sequence A received Kiovig in Period 1 and I10E in period 2. |                |
| Reporting group title                                                                                                   | Sequence B arm |
| Reporting group description:<br>The patients randomized in Sequence B received I10E in Period 1 and Kiovig in period 2. |                |

| Reporting group values                | Sequence A arm | Sequence B arm | Total |
|---------------------------------------|----------------|----------------|-------|
| Number of subjects                    | 12             | 10             | 22    |
| Age categorical<br>Units: Subjects    |                |                |       |
| Adults (18-79 years)                  | 12             | 10             | 22    |
| Age continuous<br>Units: years        |                |                |       |
| arithmetic mean                       | 49.8           | 48.3           |       |
| full range (min-max)                  | 32 to 78       | 31 to 64       | -     |
| Gender categorical<br>Units: Subjects |                |                |       |
| Female                                | 1              | 2              | 3     |
| Male                                  | 11             | 8              | 19    |

### Subject analysis sets

|                            |                                     |
|----------------------------|-------------------------------------|
| Subject analysis set title | Modified Intent-To-Treat set Kiovig |
| Subject analysis set type  | Modified intention-to-treat         |

Subject analysis set description:

The modified intent-to-treat (mITT) population was defined as all randomized subjects who received at least one administration of IMP, with the baseline and at least one post treatment MMRC efficacy assessment available. The EOS visit assessment constituted a valid post treatment assessment for this definition.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Modified Intent-To-Treat set I10E |
| Subject analysis set type  | Modified intention-to-treat       |

Subject analysis set description:

The modified intent-to-treat (mITT) population was defined as all randomized subjects who received at least one administration of IMP, with the baseline and at least one post treatment MMRC efficacy assessment available. The EOS visit assessment constituted a valid post treatment assessment for this definition.

|                            |                   |
|----------------------------|-------------------|
| Subject analysis set title | Total treated set |
| Subject analysis set type  | Safety analysis   |

Subject analysis set description:

Total treated set is defined as all subjects who received at least one administration of IMP

| Reporting group values | Modified Intent-To-Treat set Kiovig | Modified Intent-To-Treat set I10E | Total treated set |
|------------------------|-------------------------------------|-----------------------------------|-------------------|
| Number of subjects     | 21                                  | 22                                | 22                |

|                      |          |          |          |
|----------------------|----------|----------|----------|
| Age categorical      |          |          |          |
| Units: Subjects      |          |          |          |
| Adults (18-79 years) | 21       | 22       | 22       |
| Age continuous       |          |          |          |
| Units: years         |          |          |          |
| arithmetic mean      | 48.9     | 49.1     | 49.1     |
| full range (min-max) | 31 to 78 | 31 to 78 | 31 to 78 |
| Gender categorical   |          |          |          |
| Units: Subjects      |          |          |          |
| Female               | 3        | 3        | 3        |
| Male                 | 18       | 19       | 19       |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                               |                                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                         | Sequence A arm                      |
| Reporting group description:<br>The patients randomized in Sequence A received Kiovig in Period 1 and I10E in period 2.                                                                                                                                                                                                                                       |                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                         | Sequence B arm                      |
| Reporting group description:<br>The patients randomized in Sequence B received I10E in Period 1 and Kiovig in period 2.                                                                                                                                                                                                                                       |                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                         | Sequence A arm                      |
| Reporting group description:<br>The patients randomized in Sequence A received Kiovig in Period 1 and I10E in period 2.                                                                                                                                                                                                                                       |                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                         | sequence B arm                      |
| Reporting group description:<br>The patients randomized in Sequence B received I10E in Period 1 and Kiovig in period 2.                                                                                                                                                                                                                                       |                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                         | Sequence A arm                      |
| Reporting group description:<br>The patients randomized in Sequence A received I10E during Period 2.                                                                                                                                                                                                                                                          |                                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                         | Sequence B arm                      |
| Reporting group description:<br>The patients randomized in Sequence B received Kiovig during period 2.                                                                                                                                                                                                                                                        |                                     |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                    | Modified Intent-To-Treat set Kiovig |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                     | Modified intention-to-treat         |
| Subject analysis set description:<br>The modified intent-to-treat (mITT) population was defined as all randomized subjects who received at least one administration of IMP, with the baseline and at least one post treatment MMRC efficacy assessment available. The EOS visit assessment constituted a valid post treatment assessment for this definition. |                                     |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                    | Modified Intent-To-Treat set I10E   |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                     | Modified intention-to-treat         |
| Subject analysis set description:<br>The modified intent-to-treat (mITT) population was defined as all randomized subjects who received at least one administration of IMP, with the baseline and at least one post treatment MMRC efficacy assessment available. The EOS visit assessment constituted a valid post treatment assessment for this definition. |                                     |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                    | Total treated set                   |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                     | Safety analysis                     |
| Subject analysis set description:<br>Total treated set is defined as all subjects who received at least one administration of IMP                                                                                                                                                                                                                             |                                     |

### Primary: Mean MMRC 10 sum score during the evaluation period

|                                                                                                                                                                                                                                                                       |                                                                    |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                       | Mean MMRC 10 sum score during the evaluation period <sup>[1]</sup> |
| End point description:<br>The MMRC 10 sum score measure muscle strength in 10 muscle groups (5 in upper limbs and 5 in lower limbs) right and left. Each muscle group is scored from 0 (paralysis) to 5 (normal strength), resulting in a global score from 0 to 100. |                                                                    |
| End point type                                                                                                                                                                                                                                                        | Primary                                                            |
| End point timeframe:<br>The evaluation period started 13 weeks after the initiation of each product and lasted until the end of the respective period.                                                                                                                |                                                                    |

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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: The linear mixed model used in this study estimated the effects of the products, periods and sequence on the mean MMRC 10 sumscore. The estimates of the effect of each of these 3 factors were adjusted based on the 2 other factors and on the baseline values. The estimated 95% confidence interval was also calculated for these 3 factors.

The non-inferiority of I10E compared to Kiovig was tested at 1-sided alfa risk of 2.5%. The non-inferiority margin was of 2 points.

| <b>End point values</b>              | Modified<br>Intent-To-Treat<br>set Kiovig | Modified<br>Intent-To-Treat<br>set I10E |  |  |
|--------------------------------------|-------------------------------------------|-----------------------------------------|--|--|
| Subject group type                   | Subject analysis set                      | Subject analysis set                    |  |  |
| Number of subjects analysed          | 21                                        | 22                                      |  |  |
| Units: score (from 0 to 100)         |                                           |                                         |  |  |
| arithmetic mean (standard deviation) | 94.8 (± 7.3)                              | 94.6 (± 7.8)                            |  |  |

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first administration of the IMP to the end-of-study visit

Adverse event reporting additional description:

All the adverse events that occurred in at least 5% of patients (i.e. in at least 2 patients among 22)

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 16 |
|--------------------|----|

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | Kiovig group |
|-----------------------|--------------|

Reporting group description: -

|                       |            |
|-----------------------|------------|
| Reporting group title | I10E group |
|-----------------------|------------|

Reporting group description: -

| Serious adverse events                            | Kiovig group   | I10E group     |  |
|---------------------------------------------------|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 21 (0.00%) | 0 / 22 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    | 0              | 0              |  |

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

| Non-serious adverse events                            | Kiovig group     | I10E group       |  |
|-------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 15 / 21 (71.43%) | 16 / 22 (72.73%) |  |
| Vascular disorders                                    |                  |                  |  |
| Hypertension                                          |                  |                  |  |
| alternative assessment type: Systematic               |                  |                  |  |
| subjects affected / exposed                           | 0 / 21 (0.00%)   | 3 / 22 (13.64%)  |  |
| occurrences (all)                                     | 0                | 3                |  |
| Nervous system disorders                              |                  |                  |  |
| Headache                                              |                  |                  |  |
| subjects affected / exposed                           | 10 / 21 (47.62%) | 8 / 22 (36.36%)  |  |
| occurrences (all)                                     | 23               | 22               |  |
| Sciatica                                              |                  |                  |  |

|                                                                                                                                                                                                                                                                                                                                           |                                                                           |                                                                            |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                          | 2 / 21 (9.52%)<br>2                                                       | 0 / 22 (0.00%)<br>0                                                        |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)<br><br>Gait disturbances<br>subjects affected / exposed<br>occurrences (all)<br><br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 21 (9.52%)<br>2<br><br>1 / 21 (4.76%)<br>1<br><br>1 / 21 (4.76%)<br>1 | 5 / 22 (22.73%)<br>6<br><br>1 / 22 (4.55%)<br>1<br><br>1 / 22 (4.55%)<br>1 |  |
| Blood and lymphatic system disorders<br>Leukopenia<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                      | 1 / 21 (4.76%)<br>3                                                       | 1 / 22 (4.55%)<br>1                                                        |  |
| Gastrointestinal disorders<br>Nausea<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                    | 1 / 21 (4.76%)<br>1                                                       | 2 / 22 (9.09%)<br>4                                                        |  |
| Musculoskeletal and connective tissue<br>disorders<br>Muscle spasms<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)<br><br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)<br><br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Back pain | 2 / 21 (9.52%)<br>3<br><br>2 / 21 (9.52%)<br>2<br><br>0 / 21 (0.00%)<br>0 | 2 / 22 (9.09%)<br>3<br><br>2 / 22 (9.09%)<br>2<br><br>2 / 22 (9.09%)<br>2  |  |

|                                                                                                                                                  |                      |                      |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                 | 0 / 21 (0.00%)<br>0  | 2 / 22 (9.09%)<br>2  |  |
| Infections and infestations<br>nasopharyngitis<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all) | 3 / 21 (14.29%)<br>3 | 3 / 22 (13.64%)<br>3 |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                                                                                    | 1 / 21 (4.76%)<br>1  | 2 / 22 (9.09%)<br>2  |  |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                                                                              | 1 / 21 (4.76%)<br>1  | 1 / 22 (4.55%)<br>1  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 04 September 2014 | <ul style="list-style-type: none"><li>- The inclusion of subjects who received Kiovig more than 6 months before enrolment was permitted.</li><li>- The definition of the PPS population was modified to be more conservative.</li><li>- The limitation to 4 subjects per site was withdrawn to help enrol one or two more subjects in a few sites.</li><li>- The IMP dosage reduction in obese subjects was removed because it was not appropriate during the maintenance treatment phase with IVIg.</li><li>- The enrolment period was extended until the end of 3rd quarter 2016.</li></ul>                                                                |
| 26 August 2015    | <ul style="list-style-type: none"><li>- For the replacement of non-evaluable subjects, the new subject was to undergo a new randomization rather than having the same sequence group as the replaced subject.</li><li>- Modifications on some exclusion criteria.</li><li>- The potential risks related to the IMP were aligned with the European Guideline EMA/CHMP/BPWP/94038/2007 rev. 4.</li><li>- The follow-up of AEs was clarified.</li><li>- This amendment also incorporated rephrasing for clarification and consistencies between different clinical protocols.</li><li>- This amendment also specified various administrative changes.</li></ul> |
| 18 September 2015 | A urine protein reagent strip test was added before IMP administration at all follow-up visits in subjects who had an abnormal (one cross or more) urine protein reagent strip test at screening and/or had GFR in the range of 60-80 mL/min/1.73 m <sup>2</sup> measured according to the MDRD formula.                                                                                                                                                                                                                                                                                                                                                     |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported