# Clinical trial results:
# A Randomized, Double-Blind, Placebo Controlled, Cross-over Study of the Effectiveness of Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for the Treatment of Multifocal Motor Neuropathy

## Summary

| | |
|---|---|
| EudraCT number | 2009-013841-27 |
| Trial protocol | DK |
| Global end of trial date | 11 August 2011 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 05 March 2016 |
| First version publication date | 05 March 2016 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | 160604 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00666263 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Baxalta Innovations GmbH |
| Sponsor organisation address | Industriestrasse 67, Vienna, Austria, 1221 |
| Public contact | Clinical Trial Registries and Results Disclosure, Baxalta Innovations GmbH, ClinicalTrialsDisclosure@baxalta.com |
| Scientific contact | Clinical Trial Registries and Results Disclosure, Baxalta Innovations GmbH, ClinicalTrialsDisclosure@baxalta.com |
| Sponsor organisation name | Baxalta US Inc. |
| Sponsor organisation address | One Baxter Way, Westlake Village, United States, CA 91362 |
| Public contact | Clinical Trial Registries and Results Disclosure, Baxalta US Inc., ClinicalTrialsDisclosure@baxalta.com |
| Scientific contact | Clinical Trial Registries and Results Disclosure, Baxalta US Inc., ClinicalTrialsDisclosure@baxalta.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 | 11 August 2011 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 11 August 2011 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The aim of the current study was to evaluate the efficacy (effect on grip strength and disability) and safety/tolerability of Immune Globulin Intravenous (Human), 10% (IGIV, 10%) in subjects with Multifocal Motor Neuropathy (MMN).

Protection of trial subjects:

This study was conducted in accordance with this protocol, the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice, Title 21 of the US Code of Federal Regulations and the European Directive.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 22 August 2008 |
| 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 | Canada: 14 |
| Country: Number of subjects enrolled | Denmark: 2 |
| Country: Number of subjects enrolled | United States: 28 |
| Worldwide total number of subjects | 44 |
| EEA total number of subjects | 2 |

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) | 39 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment was conducted in the U.S., Canada, and Europe at 17 study sites. The first subject was enrolled in August 2008.

### Pre-assignment

Screening details:

Fifty unique potential subjects were enrolled (signed informed consent) at clinical study sites in North America and Europe. Six were screen failures. Therefore, 44 subjects were randomized and treated.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 50[1] |
| Number of subjects completed | 44 |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | Screen Failure: 6 |

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: The worldwide number of subjects enrolled only included subjects treated with study product (N=44) as per definition of enrolled in EudraCT (Enrolled=Treated). The number of subjects reported in the pre-assignment period includes all subjects enrolled in the study i.e. signed informed consent (N=50).

### Period 1

| | |
|---|---|
| Period 1 title | Study Part 1 (Stabilization Phase 1) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Each of the following 5 study parts was 12 weeks. 1: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 1); 2: IGIV, 10% or placebo (double-blind treatment cross-over period 1); 3: Open-label treatment/stabilization with IGIV, 10% (Stabilization Phase 2); 4: IGIV, 10% or placebo (double-blind treatment cross-over period 2); 5: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 3). Placebo was 0.25% human albumin.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods) |

Arm description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks (Stabilization Phase 1).

Includes all subjects who received IGIV, 10% during Study Part 2 (double-blind treatment cross-over Period 1) and Placebo during Study Part 4 (double-blind treatment cross-over Period 2).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and

increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| **Arm title** | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|

Arm description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks (Stabilization Phase 1).

Includes all subjects who received Placebo during Study Part 2 (double-blind treatment cross-over Period 1) and IGIV, 10% during Study Part 4 (double-blind treatment cross-over Period 2).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| **Number of subjects in period 1** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods) | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|---|
| Started | 22 | 22 |
| Completed | 22 | 21 |
| Not completed | 0 | 1 |
| Adverse event, non-fatal | - | 1 |

## Period 2

| | |
|---|---|
| Period 2 title | Study Part 2 (Cross-over Period 1) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Subject |

Blinding implementation details:

Each of the following 5 study parts was 12 weeks. 1: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 1); 2: IGIV, 10% or placebo (double-blind treatment cross-over period 1); 3: Open-label treatment/stabilization with IGIV, 10% (Stabilization Phase 2); 4: IGIV, 10% or placebo (double-blind treatment cross-over period 2); 5: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 3). Placebo was 0.25% human albumin.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods) |

Arm description:

Study Part 2: double-blind treatment cross-over period 1 for 12 weeks.
Includes all subjects who received Immune Globulin Intravenous (Human), 10% (IGIV, 10%) during this study period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| | |
|---|---|
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| | |
|---|---|
| **Arm title** | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |

Arm description:

Study Part 2: double-blind treatment cross-over period 1 for 12 weeks.
Includes all subjects who received Placebo during this study period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| | |
|---|---|
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| Number of subjects in period 2 | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods) | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|---|
| Started | 22 | 21 |
| Completed | 22 | 21 |

## Period 3

| | |
|---|---|
| Period 3 title | Study Part 3 (Stabilization Phase 2) |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Each of the following 5 study parts was 12 weeks. 1: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 1); 2: IGIV, 10% or placebo (double-blind treatment cross-over period 1); 3: Open-label treatment/stabilization with IGIV, 10% (Stabilization Phase 2); 4: IGIV, 10% or placebo (double-blind treatment cross-over period 2); 5: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 3). Placebo was 0.25% human albumin.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods |

Arm description:

Study Part 3: Stabilzation Phase 2. Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks.

Includes all subjects who received IGIV, 10% during Study Part 2 (double-blind treatment cross-over Period 1) and Placebo during Study Part 4 (double-blind treatment cross-over Period 2).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| | |
|---|---|
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| **Arm title** | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|

Arm description:

Study Part 3: Stabilzation Phase 2. Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks.

Includes all subjects who received Placebo during Study Part 2 (double-blind treatment cross-over Period 1) and IGIV, 10% during Study Part 4 (double-blind treatment cross-over Period 2).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| | |
|---|---|
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| **Number of subjects in period 3** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|---|
| Started | 22 | 21 |
| Completed | 22 | 21 |

## Period 4

| | |
|---|---|
| Period 4 title | Study Part 4 (Cross-over Period 2) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

Each of the following 5 study parts was 12 weeks. 1: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 1); 2: IGIV, 10% or placebo (double-blind treatment cross-over period 1); 3: Open-label treatment/stabilization with IGIV, 10% (Stabilization Phase 2); 4: IGIV, 10% or placebo (double-blind treatment cross-over period 2); 5: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 3). Placebo was 0.25% human albumin.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods |

Arm description:

Study Part 4: double-blind treatment cross-over period 2 for 12 weeks.
Includes all subjects who received Placebo during this study period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| | |
|---|---|
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| | |
|---|---|
| **Arm title** | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |

Arm description:

Study Part 4: double-blind treatment cross-over period 2 for 12 weeks.
Includes all subjects who received Immune Globulin Intravenous (Human), 10% (IGIV, 10%) during this study period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and

increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| | |
|---|---|
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| **Number of subjects in period 4** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|---|
| Started | 22 | 21 |
| Completed | 21 | 21 |
| Not completed | 1 | 0 |
| Adverse event, non-fatal | 1 | - |

## Period 5

| | |
|---|---|
| Period 5 title | Study Part 5 (Stabilization Phase 3) |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Each of the following 5 study parts was 12 weeks. 1: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 1); 2: IGIV, 10% or placebo (double-blind treatment cross-over period 1); 3: Open-label treatment/stabilization with IGIV, 10% (Stabilization Phase 2); 4: IGIV, 10% or placebo (double-blind treatment cross-over period 2); 5: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 3). Placebo was 0.25% human albumin.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods |

Arm description:

Study Part 5: Subjects received open-label treatment/stabilization with Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks (Stabilization Phase 3).

Includes all subjects who received IGIV, 10% during Study Part 2 (double-blind treatment cross-over Period 1) and Placebo during Study Part 4 (double-blind treatment cross-over Period 2).

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

| | |
|---|---|
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| | |
|---|---|
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| | |
|---|---|
| **Arm title** | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |

Arm description:

Study Part 5: Subjects received open-label treatment/stabilization with Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks (Stabilization Phase 3).

Includes all subjects who received Placebo during Study Part 2 (double-blind treatment cross-over Period 1) and IGIV, 10% during Study Part 4 (double-blind treatment cross-over Period 2).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| | |
|---|---|
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| Number of subjects in period 5 | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|---|
| Started | 21 | 21 |
| Completed | 21 | 20 |
| Not completed | 0 | 1 |
| Consent withdrawn by subject | - | 1 |

## Period 6

| | |
|---|---|
| Period 6 title | End of Study Visit |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Each of the following 5 study parts was 12 weeks. 1: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 1); 2: IGIV, 10% or placebo (double-blind treatment cross-over period 1); 3: Open-label treatment/stabilization with IGIV, 10% (Stabilization Phase 2); 4: IGIV, 10% or placebo (double-blind treatment cross-over period 2); 5: Open-label phase of treatment/stabilization with IGIV, 10% (Stabilization Phase 3). Placebo was 0.25% human albumin.

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | No |
| **Arm title** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods |

Arm description:

End of Study Visit conducted on 21 randomized subjects regardless of participation in Study Parts (except for one subject who withdrew and did not attend End of Study Visit).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| | |
|---|---|
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| | |
|---|---|
| **Arm title** | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |

| Arm description: | |
|---|---|
| End of Study Visit done on all 22 randomized subjects regardless of participation in Study Parts. | |
| Arm type | Experimental |
| Investigational medicinal product name | Placebo - 0.25% Albumin (Human) Solution |
| Investigational medicinal product code | |
| Other name | BUMINATE or Human Albumin 200 g/L Baxter Solution for Infusion |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used. Placebo administred at the same volume as IGIV, 10% that the subject received before being randomized.

| | |
|---|---|
| Investigational medicinal product name | IGIV, 10% |
| Investigational medicinal product code | |
| Other name | GAMMARGARD LIQUID (US, Canada), KIOVIG (EU) |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Immune globulin intravenous (Human), 10% (IGIV, 10%) solution consists of 1 vial of a liquid solution containing 100 mg/mL protein, of which at least 98% is Immunoglobulin (IgG). Subjects were dosed intravenously at increasing rates of infusion starting at 0.5 mL/kg body weight/hour (BM/h) and increasing to a maximum rate of 5.0 mL/kg BW/h. Alternatively Institutional Standardized Infusion Rate Protocols may be used. Rate of infusion could be adjusted at the investigator's discretion.

| **Number of subjects in period 6** | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|---|
| Started | 21 | 22 |
| Completed | 21 | 22 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Study Part 1 (Stabilization Phase 1) |
| Reporting group description:<br>Study Part 1 (Stabilization Phase 1) | |

| Reporting group values | Study Part 1 (Stabilization Phase 1) | Total | |
|---|---|---|---|
| Number of subjects | 44 | 44 | |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br><br>Units: years<br>arithmetic mean<br>standard deviation | <br><br><br>51.64<br>± 10.25 | <br><br><br><br>- | |
| Gender categorical<br><br>Units: Subjects | | | |
| Female | 12 | 12 | |
| Male | 32 | 32 | |

## End points

### End points reporting groups

| Reporting group title | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods) |
|---|---|

Reporting group description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks (Stabilization Phase 1).

Includes all subjects who received IGIV, 10% during Study Part 2 (double-blind treatment cross-over Period 1) and Placebo during Study Part 4 (double-blind treatment cross-over Period 2).

| Reporting group title | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|

Reporting group description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks (Stabilization Phase 1).

Includes all subjects who received Placebo during Study Part 2 (double-blind treatment cross-over Period 1) and IGIV, 10% during Study Part 4 (double-blind treatment cross-over Period 2).

| Reporting group title | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods) |
|---|---|

Reporting group description:

Study Part 2: double-blind treatment cross-over period 1 for 12 weeks.
Includes all subjects who received Immune Globulin Intravenous (Human), 10% (IGIV, 10%) during this study period.

| Reporting group title | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|

Reporting group description:

Study Part 2: double-blind treatment cross-over period 1 for 12 weeks.
Includes all subjects who received Placebo during this study period.

| Reporting group title | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods |
|---|---|

Reporting group description:

Study Part 3: Stabilzation Phase 2. Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks.

Includes all subjects who received IGIV, 10% during Study Part 2 (double-blind treatment cross-over Period 1) and Placebo during Study Part 4 (double-blind treatment cross-over Period 2).

| Reporting group title | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|

Reporting group description:

Study Part 3: Stabilzation Phase 2. Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks.

Includes all subjects who received Placebo during Study Part 2 (double-blind treatment cross-over Period 1) and IGIV, 10% during Study Part 4 (double-blind treatment cross-over Period 2).

| Reporting group title | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods |
|---|---|

Reporting group description:

Study Part 4: double-blind treatment cross-over period 2 for 12 weeks.
Includes all subjects who received Placebo during this study period.

| Reporting group title | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |
|---|---|

Reporting group description:

Study Part 4: double-blind treatment cross-over period 2 for 12 weeks.
Includes all subjects who received Immune Globulin Intravenous (Human), 10% (IGIV, 10%) during this study period.

| Reporting group title | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods |
|---|---|

Reporting group description:

Study Part 5: Subjects received open-label treatment/stabilization with Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks (Stabilization Phase 3).

Includes all subjects who received IGIV, 10% during Study Part 2 (double-blind treatment cross-over Period 1) and Placebo during Study Part 4 (double-blind treatment cross-over Period 2).

| | |
|---|---|
| Reporting group title | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |

Reporting group description:

Study Part 5: Subjects received open-label treatment/stabilization with Immune Globulin Intravenous (Human), 10% (IGIV, 10%) for 12 weeks (Stabilization Phase 3).

Includes all subjects who received Placebo during Study Part 2 (double-blind treatment cross-over Period 1) and IGIV, 10% during Study Part 4 (double-blind treatment cross-over Period 2).

| | |
|---|---|
| Reporting group title | Arm 1: IGIV, 10% then Placebo (During Cross-Over Periods |

Reporting group description:

End of Study Visit conducted on 21 randomized subjects regardless of participation in Study Parts (except for one subject who withdrew and did not attend End of Study Visit).

| | |
|---|---|
| Reporting group title | Arm 2: Placebo then IGIV, 10% (During Cross-Over Periods) |

Reporting group description:

End of Study Visit done on all 22 randomized subjects regardless of participation in Study Parts.

| | |
|---|---|
| Subject analysis set title | Before Stabilization 1 - All Subjects |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Baseline Measurements

| | |
|---|---|
| Subject analysis set title | End of Stabilization 1 - All Subjects |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Immune Globulin Intravenous (Human), 10% (IGIV, 10%)

| | |
|---|---|
| Subject analysis set title | End of Cross-Over 1 - All Subjects |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Either Immune Globulin Intravenous (Human), 10% (IGIV, 10%) or Placebo

| | |
|---|---|
| Subject analysis set title | End of Stabilization 2 - All Subjects |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Immune Globulin Intravenous (Human), 10% (IGIV, 10%)

| | |
|---|---|
| Subject analysis set title | End of Cross-Over 2 - All Subjects |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Either Immune Globulin Intravenous (Human), 10% (IGIV, 10%) or Placebo. The opposite of the end of Cross-Over 1.

| | |
|---|---|
| Subject analysis set title | End of Stabilization 3 - All Subjects |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Immune Globulin Intravenous (Human), 10% (IGIV, 10%)

| | |
|---|---|
| Subject analysis set title | End of Study - All Subjects |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Subjects returned following last infusion cycle (2,3, or 4 weeks after last infusion during Stabilization 3) for an End-of-Study visit for assessments including; efficacy (eg: grip strength and disability assessments), adverse events collection, physical examination, laboratory and vital signs, collection and review of diaries and other assessments.

| | |
|---|---|
| Subject analysis set title | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Cross-over Period 1 |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) (Stabilization Phase 1) all subjects; Study Part 2: IGIV, 10% (double-blind treatment cross-over Period 1); Study Part 3: Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 2); Study Part 4: Placebo (0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was

used) (double-blind treatment cross-over Period 2); Study Part 5: Subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 3).

| Subject analysis set title | Arm 1: IGIV, 10% Then Placebo- Placebo Cross-over Period 2 |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) (Stabilization Phase 1) all subjects; Study Part 2: IGIV, 10% (double-blind treatment cross-over Period 1); Study Part 3: Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 2); Study Part 4: Placebo (0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used) (double-blind treatment cross-over Period 2); Study Part 5: Subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 3).

| Subject analysis set title | Arm 2: Placebo Then IGIV, 10% - Placebo Cross-over Period 1 |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) (Stabilization Phase 1) all subjects; Study Part 2: Placebo (0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used) (double-blind treatment cross-over Period 1); Study Part 3: Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 2); Study Part 4: IGIV, 10% (double-blind treatment cross-over Period 2); Study Part 5: Subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 3).

| Subject analysis set title | Arm 2: Placebo Then IGIV, 10% - IGIV, 10% Cross-over Period 2 |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) (Stabilization Phase 1) all subjects; Study Part 2: Placebo (0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used) (double-blind treatment cross-over Period 1); Study Part 3: Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 2); Study Part 4: IGIV, 10% (double-blind treatment cross-over Period 2); Study Part 5: Subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 3).

| Subject analysis set title | Deterioration After IGIV, 10% and Placebo |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects with deterioration in Guy's Neurological Disability Scale (GNDS) scores after Immune Globulin Intravenous (Human), 10% (IGIV, 10%) and Placebo.

| Subject analysis set title | Deterioration After Placebo, But Not IGIV, 10% |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects with deterioration in Guy's Neurological Disability Scale (GNDS) scores after Placebo, but not Immune Globulin Intravenous (Human), 10% (IGIV, 10%) .

| Subject analysis set title | Deterioration After IGIV, 10%, But Not Placebo |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects with deterioration in Guy's Neurological Disability Scale (GNDS) scores after Immune Globulin Intravenous (Human), 10% (IGIV, 10%), but not Placebo.

| Subject analysis set title | No Deterioration After IGIV, 10% or Placebo |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects with no deterioration in Guy's Neurological Disability Scale (GNDS) scores after Immune Globulin Intravenous (Human), 10% (IGIV, 10%) or Placebo.

| Subject analysis set title | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) (Stabilization Phase 1) all subjects; Study Part 2: IGIV, 10% (double-blind treatment cross-over Period 1); Study Part 3: Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 2); Study Part 4: Placebo (0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used) (double-blind treatment cross-over Period 2); Study Part 5: Subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 3).

| | |
|---|---|
| Subject analysis set title | Arm 1: IGIV, 10% Then Placebo- Placebo Period |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) (Stabilization Phase 1) all subjects; Study Part 2: IGIV, 10% (double-blind treatment cross-over Period 1); Study Part 3: Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 2); Study Part 4: Placebo (0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used) (double-blind treatment cross-over Period 2); Study Part 5: Subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 3).

| | |
|---|---|
| Subject analysis set title | Arm 2: Placebo Then IGIV, 10%- Placebo Period |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) (Stabilization Phase 1) all subjects; Study Part 2: Placebo (0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used) (double-blind treatment cross-over Period 1); Study Part 3: Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 2); Study Part 4: IGIV, 10% (double-blind treatment cross-over Period 2); Study Part 5: Subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 3).

| | |
|---|---|
| Subject analysis set title | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Study Part 1: Open-label phase of treatment/stabilization on Immune Globulin Intravenous (Human), 10% (IGIV, 10%) (Stabilization Phase 1) all subjects; Study Part 2: Placebo (0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used) (double-blind treatment cross-over Period 1); Study Part 3: Between the two double-blind treatment cross-over periods, subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 2); Study Part 4: IGIV, 10% (double-blind treatment cross-over Period 2); Study Part 5: Subjects received open-label treatment/stabilization with IGIV, 10% for 12 weeks (Stabilization Phase 3).

| | |
|---|---|
| Subject analysis set title | Decline Only During IGIV, 10% |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects who experienced a relative decrease in grip strength of ≥30% in the more affected hand relative to baseline following Immune Globulin Intravenous (Human), 10% (IGIV, 10%), but not after Placebo.

| | |
|---|---|
| Subject analysis set title | Decline Only During Placebo |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects who experienced a relative decrease in grip strength of ≥30% in the more affected hand relative to baseline following the placebo, but not after Immune Globulin Intravenous (Human), 10% (IGIV, 10%).

| | |
|---|---|
| Subject analysis set title | Decline During Both Placebo and IGIV, 10% |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects who experienced a relative decrease in grip strength of ≥30% in the more affected hand relative to baseline following Immune Globulin Intravenous (Human), 10% (IGIV, 10%) %, and Placebo.

| | |
|---|---|
| Subject analysis set title | No Decline During Placebo and IGIV, 10% |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects who did not experience a relative decrease in grip strength of ≥30% in the more affected hand relative to baseline following Immune Globulin Intravenous (Human), 10% (IGIV, 10%), and Placebo.

| Subject analysis set title | Accelerated Switch During IGIV, 10% and Placebo |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects who required a switch to open label IGIV, 10% when receiving Immune Globulin Intravenous (Human), 10% (IGIV, 10%), and Placebo.

| Subject analysis set title | Accelerated Switch During Placebo, But Not IGIV, 10% |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects who required a switch to open label Immune Globulin Intravenous (Human), 10% (IGIV, 10%) when receiving Placebo, but not during IGIV, 10%.

| Subject analysis set title | Accelerated Switch During IGIV, 10%, But Not Placebo |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects who required a switch to open label Immune Globulin Intravenous (Human), 10% (IGIV, 10%) when receiving IGIV, 10%, but not during Placebo.

| Subject analysis set title | No Accelerated Switch During IGIV, 10% or Placebo |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subjects who did not require a switch to open label Immune Globulin Intravenous (Human), 10% (IGIV, 10%) when receiving IGIV, 10%, or Placebo.

## Primary: Grip Strength in the More Affected Hand

| End point title | Grip Strength in the More Affected Hand[1] |
|---|---|

End point description:

The grip strength was measured using a DynEx digital dynamometer. The result of grip strength was recorded to a resolution of 0.1 kg. Each grip strength test consisted of 3 maximal repeated contractions (trials). Each subject will perform 2 sessions of grip strength testing. After a 10-minute break, the testing session will be repeated for a total of 6 grip repetitions per hand.

Population: Intent To Treat.

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

End point timeframe:

Week 0, then at Last infusion cycle for each study part (Day 8 of last treatment cycle for 2-week interval or Day 15 of last treatment cycle for 3 or 4 -week interval), then at the end of study visit

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: Per protocol, only descriptive statistics were collected for this endpoint.

| **End point values** | Before Stabilization 1 - All Subjects | End of Stabilization 1 - All Subjects | End of Cross-Over 1 - All Subjects | End of Stabilization 2 - All Subjects |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 44 | 42 | 43 |
| Units: kilograms | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 18.14 (9.3 to 30.43) | 21.68 (14.05 to 30.83) | 19.54 (10.15 to 29.15) | 19.39 (12.75 to 33.25) |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 13.17 (5.3 to 20.08) | 14.17 (8.08 to 27.47) | 8.38 (4.86 to 17.03) | 14.18 (7.6 to 27.35) |

| End point values | End of Cross-Over 2 - All Subjects | End of Stabilization 3 - All Subjects | End of Study - All Subjects | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 43 | 36 | 43 | |
| Units: kilograms | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 11.28 (5.5 to 25.92) | 17.77 (9.23 to 27.07) | 17.37 (10.8 to 29.03) | |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 15.98 (10.73 to 29.65) | 14.28 (9.47 to 28.25) | 14 (7.48 to 24.82) | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Mean Relative Change in Grip Strength in the More Affected Hand

| End point title | Mean Relative Change in Grip Strength in the More Affected Hand[2] |
|---|---|

End point description:

Relative Change is defined as 100 * (End of the Cross-Over Period - baseline of Cross-Over Period) divided by baseline of Cross-Over Period. The grip strength was measured using a DynEx digital dynamometer. The result of grip strength was recorded to a resolution of 0.1 kg. For statistical analysis, the mean of (usually three) trials for cross-over sessions 1 and 2 was computed and the mean of the sessions was used in the analysis as the result of the grip strength measurement. Only if no grip strength testing could be performed the results were considered as missing.

Population: Intent To Treat.

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

End point timeframe:

Baseline and last infusion cycle during the two study cross-over periods, approximately weeks 13 and 24; and weeks 37 and 48 (i.e. baseline and end of Study Parts 2 and 4)

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: Currently unable to enter statistical analysis due to limitation of EudraCT. Statistics are available for these study results in ClinicalTrials.gov (NCT00666263).

| End point values | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Cross-over Period 1 | Arm 1: IGIV, 10% Then Placebo- Placebo Cross-over Period 2 | Arm 2: Placebo Then IGIV, 10% - Placebo Cross-over Period 1 | Arm 2: Placebo Then IGIV, 10% - IGIV, 10% Cross-over Period 2 |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 20 | 21 |
| Units: Percent change in grip strength | | | | |
| arithmetic mean (confidence interval 95%) | -16.36 (-30.92 to -1.8) | -30.52 (-43.68 to -17.36) | -30.11 (-48.41 to -11.81) | 23.86 (-23.11 to 70.83) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Co-Primary Endpoint: Guy's Neurological Disability Score (GNDS) for Upper Limbs

| End point title | Co-Primary Endpoint: Guy's Neurological Disability Score (GNDS) for Upper Limbs[3] |
|---|---|

End point description:

GNDS (based on Sharrack and Hughes, 1999) for the upper limbs were integers 0 to 5, with 0 indicating no impairment.

Population: Intent To Treat.

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

End point timeframe:

Week 0, then at Last infusion cycle for each study part (Day 8 of last treatment cycle for 2-week interval or Day 15 of last treatment cycle for 3 or 4 -week interval), then at the end of study visit

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: Per protocol, only descriptive statistics were collected for this endpoint.

| End point values | Before Stabilization 1 - All Subjects | End of Stabilization 1 - All Subjects | End of Cross-Over 1 - All Subjects | End of Stabilization 2 - All Subjects |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 44 | 42 | 43 |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 2 (2 to 3) | 2 (2 to 2) | 2 (2 to 2) | 2 (2 to 3) |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 2 (2 to 3) | 2 (2 to 3) | 2 (2 to 3) | 2 (1 to 3) |

| End point values | End of Cross-Over 2 - All Subjects | End of Stabilization 3 - All Subjects | End of Study - All Subjects | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 43 | 36 | 43 | |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 2.5 (2 to 3) | 2 (2 to 2) | 2 (2 to 2) | |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 2 (2 to 3) | 2 (2 to 3) | 2 (2 to 3) | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Co-Primary Endpoint: Proportion of Subjects with Deterioration in Guy's Neurological Disability Score (GNDS)

| End point title | Co-Primary Endpoint: Proportion of Subjects with Deterioration in Guy's Neurological Disability Score (GNDS)[4] |
|---|---|

End point description:

GNDS (based on Sharrack and Hughes, 1999) for the upper limbs were integers 0 to 5, with 0 indicating no impairment.

Population: Intent To Treat.

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

End point timeframe:

Baseline and last infusion cycle during the two study cross-over periods, approximately weeks 13 and 24; and weeks 37 and 48 (i.e. baseline and end of Study Parts 2 and 4)

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: Currently unable to enter statistical analysis due to limitation of EudraCT. Statistics are available for these study results in ClinicalTrials.gov (NCT00666263).

| **End point values** | Deterioration After IGIV, 10% and Placebo | Deterioration After Placebo, But Not IGIV, 10% | Deterioration After IGIV, 10%, But Not Placebo | No Deterioration After IGIV, 10% or Placebo |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 42 | 42 | 42 | 42 |
| Units: Proportion of subjects | | | | |
| number (not applicable) | 4.8 | 35.7 | 11.9 | 47.6 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Rate of temporally associated adverse events (AEs) per infusion

| End point title | Rate of temporally associated adverse events (AEs) per infusion[5] |
|---|---|

End point description:

The total number of all AEs which begin during or within 72 hours of completion of an infusion, irrespective of being related or not related to the study product (IGIV, 10% or Placebo), divided by the total number of infusions, and multiplied by 100.

Population: Safety Dataset.

Number of infusions [N] analyzed per subject analysis set is as follows:
Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period N=104;
Arm 1: IGIV, 10% Then Placebo- Placebo Period N=68;
Arm 2: Placebo Then IGIV, 10%- Placebo Period N=61;
Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period N=138.

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

End point timeframe:

Within 72 hours of completion of an infusion during the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

Notes:

[5] - 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: Per protocol, only descriptive statistics were collected for this endpoint.

| End point values | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period | Arm 1: IGIV, 10% Then Placebo- Placebo Period | Arm 2: Placebo Then IGIV, 10%- Placebo Period | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 21 | 21 |
| Units: Percentage of AEs per infusion | | | | |
| number (not applicable) | 11.5 | 13.2 | 24.6 | 11.6 |

### Statistical analyses

No statistical analyses for this end point

## Primary: The percentage of subjects for whom the infusion rate of any infusion was reduced and/or the infusion was interrupted or stopped for any reason

| End point title | The percentage of subjects for whom the infusion rate of any infusion was reduced and/or the infusion was interrupted or stopped for any reason[6] |
|---|---|

End point description:

Population: Safety Dataset.

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

End point timeframe:

Throughout the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

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: Per protocol, only descriptive statistics were collected for this endpoint.

| End point values | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period | Arm 1: IGIV, 10% Then Placebo- Placebo Period | Arm 2: Placebo Then IGIV, 10%- Placebo Period | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 21 | 21 |
| Units: percentage of subjects | | | | |
| number (not applicable) | 9.1 | 0 | 4.8 | 4.8 |

### Statistical analyses

No statistical analyses for this end point

## Primary: The percentage of infusions for which the infusion rate was reduced and/or the infusion was interrupted or stopped for any reason

| End point title | The percentage of infusions for which the infusion rate was reduced and/or the infusion was interrupted or stopped for any reason[7] |
|---|---|

End point description:

Number of infusions [N] analyzed per subject analysis set is as follows:
Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period N=104;
Arm 1: IGIV, 10% Then Placebo- Placebo Period N=68;

Arm 2: Placebo Then IGIV, 10%- Placebo Period N=61;
Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period N=138.

Population: Safety Dataset.

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

End point timeframe:

Throughout the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

Notes:

[7] - 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: Per protocol, only descriptive statistics were collected for this endpoint.

| **End point values** | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period | Arm 1: IGIV, 10% Then Placebo- Placebo Period | Arm 2: Placebo Then IGIV, 10%- Placebo Period | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 21 | 21 |
| Units: percentage of infusions | | | | |
| number (not applicable) | 2.9 | 0 | 1.6 | 0.7 |

## Statistical analyses

No statistical analyses for this end point

## Primary: The percentage of subjects reporting one or more moderate or severe AEs that began during infusion or within 72 hours of completion of an infusion

| End point title | The percentage of subjects reporting one or more moderate or severe AEs that began during infusion or within 72 hours of completion of an infusion[8] |
|---|---|

End point description:

Population: Safety Dataset.

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

End point timeframe:

Within 72 hours of completion of an infusion during the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

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: Per protocol, only descriptive statistics were collected for this endpoint.

| **End point values** | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period | Arm 1: IGIV, 10% Then Placebo- Placebo Period | Arm 2: Placebo Then IGIV, 10%- Placebo Period | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 21 | 21 |
| Units: percentage of subjects | | | | |
| number (not applicable) | 4.5 | 27.3 | 19 | 4.8 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with at least a 30% decline in relative grip strength in the more affected hand (measured using a DynEx digital dynamometer)

| End point title | Percentage of subjects with at least a 30% decline in relative grip strength in the more affected hand (measured using a DynEx digital dynamometer) |
|---|---|

End point description:

Relative grip strength change is defined as 100 * (End of the Cross-Over Period - baseline of Cross-Over Period) divided by baseline of Cross-Over Period. The grip strength was measured using a DynEx digital dynamometer. The result of grip strength was recorded to a resolution of 0.1 kg. For statistical analysis, the mean of (usually three) trials for cross-over sessions 1 and 2 was computed and the mean of the sessions was used in the analysis as the result of the grip strength measurement. Only if no grip strength testing could be performed the results were considered as missing.

Population: Intent to Treat.

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

End point timeframe:

Baseline and last infusion cycle during the two study cross-over periods, approximately weeks 13 and 24; and weeks 37 and 48 (i.e. baseline and end of Study Parts 2 and 4)

| **End point values** | Decline Only During IGIV, 10% | Decline Only During Placebo | Decline During Both Placebo and IGIV, 10% | No Decline During Placebo and IGIV, 10% |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 42 | 42 | 42 | 42 |
| Units: Percentage of subjects | | | | |
| number (not applicable) | 4.8 | 42.9 | 4.8 | 47.6 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Grip Strength in the Less Affected Hand

| End point title | Grip Strength in the Less Affected Hand |
|---|---|

End point description:

The grip strength was measured using a DynEx digital dynamometer. The result of grip strength was recorded to a resolution of 0.1 kg. Each grip strength test consisted of 3 maximal repeated contractions (trials). Each subject will perform 2 sessions of grip strength testing. After a 10-minute break, the testing session will be repeated for a total of 6 grip repetitions per hand.

Population: Intent to Treat.

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

End point timeframe:

Week 0, then at Last infusion cycle for each study part (Day 8 of last treatment cycle for 2-week interval or Day 15 of last treatment cycle for 3 or 4 -week interval), then at the end of study visit

| End point values | Before Stabilization 1 - All Subjects | End of Stabilization 1 - All Subjects | End of Cross-Over 1 - All Subjects | End of Stabilization 2 - All Subjects |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 44 | 42 | 43 |
| Units: kilograms | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 27.98 (22.35 to 36.35) | 29.52 (23.28 to 36.98) | 29.79 (20.48 to 37.88) | 29.17 (21.68 to 37.7) |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 27.23 (18.73 to 34.45) | 28.23 (19.72 to 36.8) | 20.28 (9.61 to 33.44) | 26.92 (17.52 to 37.72) |

| End point values | End of Cross-Over 2 - All Subjects | End of Stabilization 3 - All Subjects | End of Study - All Subjects | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 43 | 36 | 43 | |
| Units: kilograms | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 26.58 (13.67 to 32.83) | 28.97 (15.95 to 34.38) | 29.68 (14.72 to 34.35) | |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 27.35 (21.58 to 37.12) | 25.72 (20.18 to 36.55) | 24.98 (16.02 to 35.85) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Relative Change in Grip Strength in the Less Affected Hand

| End point title | Mean Relative Change in Grip Strength in the Less Affected Hand |
|---|---|

End point description:

Relative Change is defined as 100 * (End of the Cross-Over Period - Baseline of Cross-Over Period) divided by baseline of Cross-Over Period. The grip strength was measured using a DynEx digital dynamometer. The result of grip strength was recorded to a resolution of 0.1 kg. For statistical analysis, the mean of (usually three) trials for cross-over sessions 1 and 2 was computed and the mean of the sessions was used in the analysis as the result of the grip strength measurement. Only if no grip strength testing could be performed the results were considered as missing.

Population: Intent to Treat.

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

End point timeframe:

Baseline and last infusion cycle during the two study cross-over periods, approximately weeks 13 and 24; and weeks 37 and 48 (i.e. baseline and end of Study Parts 2 and 4)

| End point values | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Cross-over Period 1 | Arm 1: IGIV, 10% Then Placebo-Placebo Cross-over Period 2 | Arm 2: Placebo Then IGIV, 10% - Placebo Cross-over Period 1 | Arm 2: Placebo Then IGIV, 10% - IGIV, 10% Cross-over Period 2 |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 20 | 21 |
| Units: Percent change in grip strength | | | | |
| arithmetic mean (confidence interval 95%) | -2.52 (-7.9 to 2.85) | -17.96 (-29.81 to -6.1) | -29.22 (-40.62 to -17.83) | 19.67 (-10.84 to 50.17) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Proportion of Subjects That Were Accelerated Forward into the Next Stabilization Phase (ie Switched to Open-Label IGIV, 10%)

| End point title | Proportion of Subjects That Were Accelerated Forward into the Next Stabilization Phase (ie Switched to Open-Label IGIV, 10%) |
|---|---|

End point description:

Subjects were permitted to switch from blinded treatment with placebo or IGIV, 10% to open label IGIV, 10% if they and investigator agreed that deterioration had occurred to the extent that the subject had unacceptable difficulty carrying out daily activities involving the affected muscles, or decline in grip strength of ≥50% in the more affected hand had occurred.

Population: Intent to Treat.

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

End point timeframe:

During the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

| End point values | Accelerated Switch During IGIV, 10% and Placebo | Accelerated Switch During Placebo, But Not IGIV, 10% | Accelerated Switch During IGIV, 10%, But Not Placebo | No Accelerated Switch During IGIV, 10% or Placebo |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 42 | 42 | 42 | 42 |
| Units: Proportion of subjects | | | | |
| number (not applicable) | 0 | 69 | 2.4 | 28.6 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Patient Global Impression of Change

| End point title | Patient Global Impression of Change |
|---|---|

End point description:

Patient Global Impression of Change was measured on an ordinal scale of 1-7, higher scores

representing greater perceived deterioration since the previous efficacy assessment (ranging from (1) very much improved to very much worse (7)). 1. Very much improved 2. Much improved 3. Minimally improved 4. No change 5. Minimally worse 6. Much worse 7. Very much worse.

Population: Intent to Treat.

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

End point timeframe:

Last infusion cycle for each study part (Day 8 of last treatment cycle for 2-week interval or Day 15 of last treatment cycle for 3 or 4 -week interval), then at the end of study visit

| **End point values** | End of Stabilization 1 - All Subjects | End of Cross-Over 1 - All Subjects | End of Stabilization 2 - All Subjects | End of Cross-Over 2 - All Subjects |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 42 | 43 | 43 |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV, 10% then Placebo (N= 22, 22, 22, 21, 17, 21) | 4 (3 to 4) | 4 (4 to 4) | 4 (4 to 4) | 5 (5 to 6) |
| Placebo then IGIV, 10% (N= 22, 20, 21, 21, 19, 22) | 4 (3 to 4) | 6 (5 to 6) | 3 (2 to 3) | 4 (3 to 4) |

| **End point values** | End of Stabilization 3 - All Subjects | End of Study - All Subjects | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 36 | 43 | | |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV, 10% then Placebo (N= 22, 22, 22, 21, 17, 21) | 2 (2 to 4) | 4 (3 to 4) | | |
| Placebo then IGIV, 10% (N= 22, 20, 21, 21, 19, 22) | 4 (4 to 4) | 4 (4 to 4) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Disability Sum Score

| End point title | Overall Disability Sum Score |
|---|---|

End point description:

The overall disability sum scale (based on Merkies et al., 2002) is a patient questionnaire that measures disability. Overall disability sum score = arm disability scale (range 0–5) + leg disability scale (range 0–7); Overall Range: 0 (no signs of disability) to 12 (maximum disability).

Population: Intent to Treat.

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

End point timeframe:

Week 0, then at Last infusion cycle for each study part (Day 8 of last treatment cycle for 2-week interval

or Day 15 of last treatment cycle for 3 or 4 -week interval), then at the end of study visit

| **End point values** | Before Stabilization 1 - All Subjects | End of Stabilization 1 - All Subjects | End of Cross-Over 1 - All Subjects | End of Stabilization 2 - All Subjects |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 44 | 42 | 43 |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 3 (2 to 4) | 2 (2 to 4) | 3 (2 to 4) | 2 (2 to 4) |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 3 (2 to 4) | 3 (2 to 4) | 4 (3 to 5) | 3 (2 to 4) |

| **End point values** | End of Cross-Over 2 - All Subjects | End of Stabilization 3 - All Subjects | End of Study - All Subjects | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 43 | 36 | 43 | |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 3 (2 to 4) | 2 (2 to 4) | 2 (2 to 4) | |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 3 (2 to 4) | 4 (2 to 4) | 3 (2 to 4) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Disability Sum Score - Standardized

| End point title | Overall Disability Sum Score - Standardized |
|---|---|

End point description:

The overall disability sum scale (based on Merkies et al., 2002) is a patient questionnaire that measures disability. Overall disability sum score = arm disability scale (range 0–5) + leg disability scale (range 0–7); Overall Range: 0 (no signs of disability) to 12 (maximum disability). This was standardized to a scale of 0 to 100 (the best score being 100) to allow calculation of relative changes.

Population: Intent to Treat.

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

End point timeframe:

Week 0, then at Last infusion cycle for each study part (Day 8 of last treatment cycle for 2-week interval or Day 15 of last treatment cycle for 3 or 4 -week interval), then at the end of study visit

| End point values | Before Stabilization 1 - All Subjects | End of Stabilization 1 - All Subjects | End of Cross-Over 1 - All Subjects | End of Stabilization 2 - All Subjects |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 44 | 42 | 43 |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 75 (66.7 to 83.3) | 83.3 (66.7 to 83.3) | 79.2 (66.7 to 83.3) | 83.3 (66.7 to 83.3) |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 75 (66.7 to 83.3) | 75 (66.7 to 83.3) | 66.7 (58.3 to 75) | 75 (66.7 to 83.3) |

| End point values | End of Cross-Over 2 - All Subjects | End of Stabilization 3 - All Subjects | End of Study - All Subjects | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 43 | 36 | 43 | |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 75 (66.7 to 83.3) | 83.3 (66.7 to 83.3) | 83.3 (66.7 to 83.3) | |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 75 (66.7 to 83.3) | 66.7 (66.7 to 83.3) | 75 (66.7 to 83.3) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Relative Change in Overall Disability Sum Score

| End point title | Mean Relative Change in Overall Disability Sum Score |
|---|---|

End point description:

Relative Change is defined as 100 * (End of the Cross-Over Period - baseline of Cross-Over Period) divided by baseline of Cross-Over Period. The overall disability sum scale (based on Merkies et al., 2002) is a patient questionnaire that measures disability (from 0, "no signs of disability" to 12, "most severe disability"). This was standardized to a scale of 0 to 100 (the best score being 100) to allow calculation of relative changes.

Population: Intent to Treat.

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

End point timeframe:

Baseline and last infusion cycle during the two study cross-over periods, approximately weeks 13 and 24; and weeks 37 and 48 (i.e. baseline and end of Study Parts 2 and 4)

| End point values | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Cross-over Period 1 | Arm 1: IGIV, 10% Then Placebo-Placebo Cross-over Period 2 | Arm 2: Placebo Then IGIV, 10% - Placebo Cross-over Period 1 | Arm 2: Placebo Then IGIV, 10% - IGIV, 10% Cross-over Period 2 |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 20 | 21 |
| Units: Percent change in score | | | | |
| arithmetic mean (confidence interval 95%) | -3.14 (-6.55 to 0.27) | -5.77 (-10.33 to -1.2) | -8.46 (-12.81 to -4.11) | 0.92 (-2.88 to 4.73) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time Required by Subjects to Complete the 9 Hole Peg Board Test (9-HPT) with the Dominant Hand

| End point title | Time Required by Subjects to Complete the 9 Hole Peg Board Test (9-HPT) with the Dominant Hand |
|---|---|

End point description:

The 9-HPT is a quantitative measure of upper extremity (arm and hand) function. Subjects picked up the pegs one at a time (nine in total), and put them into the holes on the board as quickly as possible, in any order until all the holes were filled. Then, without pausing, subjects removed the pegs one at a time and returned them to the container as quickly as possible. Each subject did this two times with their dominant hand. The 9-HCT objective is to see how fast subjects could put all of the pegs in and take them out again.

Population: Intent to Treat.

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

End point timeframe:

Week 0, then at Last infusion cycle for each study part (Day 8 of last treatment cycle for 2-week interval or Day 15 of last treatment cycle for 3 or 4 -week interval), then at the end of study visit

| End point values | Before Stabilization 1 - All Subjects | End of Stabilization 1 - All Subjects | End of Cross-Over 1 - All Subjects | End of Stabilization 2 - All Subjects |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 44 | 42 | 43 |
| Units: Seconds | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 20.75 (19.5 to 27.5) | 22 (19.5 to 29) | 20.25 (18 to 29) | 21 (18 to 24.5) |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 26.75 (20.5 to 39) | 25.25 (19 to 33.5) | 27.75 (23 to 43.5) | 24.5 (19 to 34.5) |

| End point values | End of Cross-Over 2 - All Subjects | End of Stabilization 3 - All Subjects | End of Study - All Subjects | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 43 | 36 | 43 | |

| | | | | |
|---|---|---|---|---|
| Units: Seconds | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 20.5 (18.5 to 27.5) | 20.5 (19 to 24.5) | 20 (19 to 25.5) | |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 25 (20 to 30.5) | 27.5 (20.5 to 35.5) | 26.25 (19.5 to 33) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Relative Change in Time Required by Subjects to Complete the 9 Hole Peg Board Test (9-HPT) With the Dominant Hand

| End point title | Mean Relative Change in Time Required by Subjects to Complete the 9 Hole Peg Board Test (9-HPT) With the Dominant Hand |
|---|---|

End point description:

Relative Change is defined as 100 * (End of the Cross-Over Period - baseline of Cross-Over Period) divided by baseline of Cross-Over Period. The 9-HPT is a quantitative measure of upper extremity (arm and hand) function. Subjects picked up the pegs one at a time (nine in total), and put them into the holes on the board as quickly as possible, in any order until all the holes were filled. Then, without pausing, subjects removed the pegs one at a time and returned them to the container as quickly as possible. Each subject did this two times with their dominant hand. The 9-HCT objective is to see how fast subjects could put all of the pegs in and take them out again.

Population: Intent to Treat.

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

End point timeframe:

Baseline and last infusion cycle during the two study cross-over periods, approximately weeks 13 and 24; and weeks 37 and 48 (i.e. baseline and end of Study Parts 2 and 4)

| **End point values** | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Cross-over Period 1 | Arm 1: IGIV, 10% Then Placebo- Placebo Cross-over Period 2 | Arm 2: Placebo Then IGIV, 10% - Placebo Cross-over Period 1 | Arm 2: Placebo Then IGIV, 10% - IGIV, 10% Cross-over Period 2 |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 20 | 21 |
| Units: Percent change in time | | | | |
| arithmetic mean (confidence interval 95%) | -2.57 (-9.99 to 4.86) | 3.9 (-4.59 to 12.39) | 29.89 (12.46 to 47.31) | 4.89 (-9.45 to 19.23) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time Required by Subjects to Complete the 9 Hole Peg Board Test (9-HPT) with the Non-Dominant Hand

| End point title | Time Required by Subjects to Complete the 9 Hole Peg Board Test (9-HPT) with the Non-Dominant Hand |
|---|---|

End point description:

The 9-HPT is a quantitative measure of upper extremity (arm and hand) function. Subjects picked up the pegs one at a time (nine in total), and put them into the holes on the board as quickly as possible, in any order until all the holes were filled. Then, without pausing, subjects removed the pegs one at a time and returned them to the container as quickly as possible. Each subject did this two times with their non-dominant hand. The 9-HCT objective is to see how fast subjects could put all of the pegs in and take them out again.

Population: Intent to Treat.

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

End point timeframe:

Week 0, then at Last infusion cycle for each study part (Day 8 of last treatment cycle for 2-week interval or Day 15 of last treatment cycle for 3 or 4 -week interval), then at the end of study visit

| **End point values** | Before Stabilization 1 - All Subjects | End of Stabilization 1 - All Subjects | End of Cross-Over 1 - All Subjects | End of Stabilization 2 - All Subjects |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 44 | 42 | 43 |
| Units: Seconds | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 25.75 (20 to 29.5) | 22.5 (19.5 to 27) | 24 (19.5 to 28.5) | 23.5 (19.5 to 27) |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 31.25 (22.5 to 51) | 28 (22.5 to 40) | 37.25 (26.25 to 82.75) | 31.5 (24 to 38.5) |

| **End point values** | End of Cross-Over 2 - All Subjects | End of Stabilization 3 - All Subjects | End of Study - All Subjects | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 43 | 36 | 43 | |
| Units: Seconds | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 25.25 (22.5 to 29.5) | 21 (19.5 to 24.5) | 23 (20.5 to 26.5) | |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 32.5 (22 to 41) | 30 (22.5 to 39.5) | 30 (21 to 38.5) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Relative Change in Time Required by Subjects to Complete the 9 Hole Peg Board Test (9-HPT) With the Non-Dominant Hand

| End point title | Mean Relative Change in Time Required by Subjects to Complete the 9 Hole Peg Board Test (9-HPT) With the Non-Dominant Hand |
|---|---|

End point description:

Relative Change is defined as 100 * (End of the Cross-Over Period - baseline of Cross-Over Period) divided by baseline of Cross-Over Period. The 9-HPT is a quantitative measure of upper extremity (arm

and hand) function. Subjects picked up the pegs one at a time (nine in total), and put them into the holes on the board as quickly as possible, in any order until all the holes were filled. Then, without pausing, subjects removed the pegs one at a time and returned them to the container as quickly as possible. Each subject did this two times with their non-dominant hand. The 9-HCT objective is to see how fast subjects could put all of the pegs in and take them out again.

Population: Intent to Treat.

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

End point timeframe:

Baseline and last infusion cycle during the two study cross-over periods, approximately weeks 13 and 24; and weeks 37 and 48 (i.e. baseline and end of Study Parts 2 and 4)

| **End point values** | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Cross-over Period 1 | Arm 1: IGIV, 10% Then Placebo-Placebo Cross-over Period 2 | Arm 2: Placebo Then IGIV, 10% - Placebo Cross-over Period 1 | Arm 2: Placebo Then IGIV, 10% - IGIV, 10% Cross-over Period 2 |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 20 | 21 |
| Units: Percent change in time | | | | |
| arithmetic mean (confidence interval 95%) | 4.78 (-1.65 to 11.21) | 13.06 (4.46 to 21.65) | 52.93 (26.82 to 79.05) | 8.56 (-4.88 to 22.01) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Subjects' Assessment of physical functioning on a Visual Analog Scale (VAS)

| End point title | Subjects' Assessment of physical functioning on a Visual Analog Scale (VAS) |
|---|---|

End point description:

The VAS measured patients’ assessment of physical functioning on a 10 centimeter scale of 0-10, on which 0 represents “no symptoms” and 10 “disabled, unable to use affected limbs”.

Population: Intent to Treat.

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

End point timeframe:

Week 0, then at Last infusion cycle for each study part (Day 8 of last treatment cycle for 2-week interval or Day 15 of last treatment cycle for 3 or 4 -week interval), then at the end of study visit

| **End point values** | Before Stabilization 1 - All Subjects | End of Stabilization 1 - All Subjects | End of Cross-Over 1 - All Subjects | End of Stabilization 2 - All Subjects |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 44 | 42 | 43 |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |

| | | | | |
|---|---|---|---|---|
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 4.8 (2.9 to 6.3) | 2.95 (1.6 to 5.1) | 4.1 (2 to 5.6) | 3.5 (1.7 to 5.1) |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 4.95 (2.3 to 7.6) | 3.15 (2.7 to 5.5) | 7.15 (6.75 to 7.6) | 5.1 (2.3 to 6.1) |

| **End point values** | End of Cross-Over 2 - All Subjects | End of Stabilization 3 - All Subjects | End of Study - All Subjects | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 43 | 36 | 43 | |
| Units: Scores on a scale | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IGIV then Placebo (N= 22, 22, 22, 22, 22, 17, 21) | 6.85 (5.9 to 8.1) | 4.5 (2.6 to 5.1) | 3.7 (1.9 to 5.4) | |
| Placebo then IGIV (N= 22, 22, 20, 21, 21, 19, 22) | 4.6 (2.4 to 5.9) | 4.5 (2.6 to 6) | 5.15 (2.8 to 6.3) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Relative Change in Subjects' Assessment of Physical Functioning on a Visual Analog Scale (VAS)

| | |
|---|---|
| End point title | Mean Relative Change in Subjects' Assessment of Physical Functioning on a Visual Analog Scale (VAS) |

End point description:

Relative Change is defined as 100 * (End of the Cross-Over Period - baseline of Cross-Over Period) divided by baseline of Cross-Over Period. The VAS measured patients’ assessment of physical functioning on a 10 centimeter scale of 0-10, on which 0 represents “no symptoms” and 10 “disabled, unable to use affected limbs”.

Population: Intent to Treat.

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

End point timeframe:

Baseline and last infusion cycle during the two study cross-over periods, approximately weeks 13 and 24; and weeks 37 and 48 (i.e. baseline and end of Study Parts 2 and 4)

| **End point values** | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Cross-over Period 1 | Arm 1: IGIV, 10% Then Placebo- Placebo Cross-over Period 2 | Arm 2: Placebo Then IGIV, 10% - Placebo Cross-over Period 1 | Arm 2: Placebo Then IGIV, 10% - IGIV, 10% Cross-over Period 2 |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 20 | 21 |
| Units: Percent change in assessment | | | | |
| arithmetic mean (confidence interval 95%) | 140.92 (-1.35 to 283.19) | 321.75 (-73.45 to 716.95) | 258.09 (-100.83 to 617.01) | 5.75 (-11.54 to 23.04) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Rate of related AEs per infusion

| End point title | Rate of related AEs per infusion |
|---|---|

End point description:

The total number of AEs determined by the investigator to be related to the study product that occur at any time during the study divided by the total number of infusions, and multiplied by 100.

Number of infusions [N] analyzed per subject analysis set is as follows:
Arm 1 - 10% Period N=104; Arm 1 - Placebo Period N=68; Arm 2 - 10% Period; Arm 2 - Placebo Period N=61; Arm 2 - 10% Period N=138.

Population: Safety Dataset.

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

End point timeframe:

Throughout the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

| End point values | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period | Arm 1: IGIV, 10% Then Placebo- Placebo Period | Arm 2: Placebo Then IGIV, 10%- Placebo Period | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 21 | 21 |
| Units: AEs per infusion | | | | |
| number (not applicable) | 4.8 | 20.6 | 44.3 | 15.9 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Rate of related SAEs per infusion

| End point title | Rate of related SAEs per infusion |
|---|---|

End point description:

The total number of SAEs determined by the investigator to be related to the study product that occur at any time during the study divided by the total number of infusions, and multiplied by 100.

Number of infusions [N] analyzed per subject analysis set is as follows:
Arm 1 - 10% Period N=104; Arm 1 - Placebo Period N=68; Arm 2 - 10% Period; Arm 2 - Placebo Period N=61; Arm 2 - 10% Period N=138.

Population: Safety Dataset.

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

End point timeframe:

Throughout the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

| **End point values** | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period | Arm 1: IGIV, 10% Then Placebo- Placebo Period | Arm 2: Placebo Then IGIV, 10%- Placebo Period | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 21 | 21 |
| Units: SAEs per infusion | | | | |
| number (not applicable) | 0 | 0 | 0 | 0.7 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: The proportion of subjects for whom the infusion rate of any infusion was reduced and/or the infusion was interrupted or stopped for tolerability concerns/AEs

| End point title | The proportion of subjects for whom the infusion rate of any infusion was reduced and/or the infusion was interrupted or stopped for tolerability concerns/AEs |
|---|---|

End point description:

Population: Safety Dataset.

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

End point timeframe:

Throughout the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

| **End point values** | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period | Arm 1: IGIV, 10% Then Placebo- Placebo Period | Arm 2: Placebo Then IGIV, 10%- Placebo Period | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 21 | 21 |
| Units: Proportion of subjects | | | | |
| number (not applicable) | 0 | 0 | 0 | 4.8 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: The proportion of infusions for which the infusion rate was reduced

**and/or the infusion was interrupted or stopped for tolerability concerns/AEs**

| End point title | The proportion of infusions for which the infusion rate was reduced and/or the infusion was interrupted or stopped for tolerability concerns/AEs |
|---|---|

End point description:

Number of infusions [N] analyzed per subject analysis set is as follows:
Arm 1 - 10% Period N=104; Arm 1 - Placebo Period N=68; Arm 2 - 10% Period; Arm 2 - Placebo Period N=61; Arm 2 - 10% Period N=138.

Population: Safety Dataset.

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

End point timeframe:

Throughout the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

| **End point values** | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period | Arm 1: IGIV, 10% Then Placebo- Placebo Period | Arm 2: Placebo Then IGIV, 10%- Placebo Period | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 21 | 21 |
| Units: proportion of infusions | | | | |
| number (not applicable) | 0 | 0 | 0 | 0.7 |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: The proportion of infusions associated with one or more AEs related to the study product**

| End point title | The proportion of infusions associated with one or more AEs related to the study product |
|---|---|

End point description:

Number of infusions [N] analyzed per subject analysis set is as follows:
Arm 1 - 10% Period N=104; Arm 1 - Placebo Period N=68; Arm 2 - 10% Period; Arm 2 - Placebo Period N=61; Arm 2 - 10% Period N=138.

Population: Safety Dataset.

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

End point timeframe:

Throughout the two study cross-over periods, approximately weeks 13-24 and weeks 37-48 (i.e. Study Parts 2 and 4)

| End point values | Arm 1: IGIV, 10% Then Placebo- IGIV, 10% Period | Arm 1: IGIV, 10% Then Placebo- Placebo Period | Arm 2: Placebo Then IGIV, 10%- Placebo Period | Arm 2: Placebo Then IGIV, 10%- IGIV, 10% Period |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 22 | 22 | 21 | 21 |
| Units: proportion of infusions | | | | |
| number (not applicable) | 3.8 | 19.1 | 34.4 | 13 |

### Statistical analyses

No statistical analyses for this end point

## Post-hoc: Proportion of subjects with at least a 30% decline in relative grip strength in the less affected hand (measured using a DynEx digital dynamometer)

| End point title | Proportion of subjects with at least a 30% decline in relative grip strength in the less affected hand (measured using a DynEx digital dynamometer) |
|---|---|

End point description:

Relative grip strength change is defined as 100 * (End of the Cross-Over Period - baseline of Cross-Over Period) divided by baseline of Cross-Over Period. The grip strength was measured using a DynEx digital dynamometer. The result of grip strength was recorded to a resolution of 0.1 kg. For statistical analysis, the mean of (usually three) trials for cross-over sessions 1 and 2 was computed and the mean of the sessions was used in the analysis as the result of the grip strength measurement. Only if no grip strength testing could be performed the results were considered as missing.

Population: Intent to Treat.

| End point type | Post-hoc |
|---|---|

End point timeframe:

Baseline and last infusion cycle during the two study cross-over periods, approximately weeks 13 and 24; and weeks 37 and 48 (i.e. baseline and end of Study Parts 2 and 4)

| End point values | Decline Only During IGIV, 10% | Decline Only During Placebo | Decline During Both Placebo and IGIV, 10% | No Decline During Placebo and IGIV, 10% |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 42 | 42 | 42 | 42 |
| Units: Proportion of subjects | | | | |
| number (not applicable) | 0 | 31 | 2.4 | 66.7 |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Throughout the study period, approximately three years. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | Not known |

| Reporting groups | |
|---|---|
| Reporting group title | IGIV, 10% |
| Reporting group description: | |
| Subjects received IGIV, 10% at the same equivalent dose per week administered prior to the study (0.4 to 2.0 g per kg BW per infusion cycle) | |
| Reporting group title | Placebo |
| Reporting group description: | |
| 0.25% human albumin: BUMINATE 25% Albumin (Human)(Baxter Healthcare Corporation) used where licensed; otherwise Human Albumin 200 g/L Baxter Solution for Infusion was used) | |

| Serious adverse events | IGIV, 10% | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 44 (4.55%) | 0 / 43 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | IGIV, 10% | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 35 / 44 (79.55%) | 33 / 43 (76.74%) | |
| Injury, poisoning and procedural complications | | | |
| CONTUSION | | | |
| subjects affected / exposed | 5 / 44 (11.36%) | 2 / 43 (4.65%) | |
| occurrences (all) | 9 | 2 | |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 16 / 44 (36.36%) | 2 / 43 (4.65%) | |
| occurrences (all) | 34 | 3 | |
| NEUROLOGICAL DECOMPENSATION | | | |
| subjects affected / exposed | 10 / 44 (22.73%) | 25 / 43 (58.14%) | |
| occurrences (all) | 10 | 25 | |
| NEUROLOGICAL SYMPTOM | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 2 / 43 (4.65%) | |
| occurrences (all) | 3 | 2 | |
| PARAESTHESIA | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 1 / 43 (2.33%) | |
| occurrences (all) | 4 | 1 | |
| SINUS HEADACHE | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 0 / 43 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| General disorders and administration site conditions | | | |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 7 / 44 (15.91%) | 1 / 43 (2.33%) | |
| occurrences (all) | 9 | 1 | |
| CHEST DISCOMFORT | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 0 / 43 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| FATIGUE | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 0 / 43 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 2 / 43 (4.65%) | |
| occurrences (all) | 3 | 2 | |

| | | | |
|---|---|---|---|
| Gastrointestinal disorders | | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 0 / 43 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| NAUSEA | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 2 / 43 (4.65%) | |
| occurrences (all) | 31 | 3 | |
| TOOTHACHE | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 0 / 43 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 7 / 44 (15.91%) | 0 / 43 (0.00%) | |
| occurrences (all) | 8 | 0 | |
| SINUS CONGESTION | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 0 / 43 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 8 / 44 (18.18%) | 2 / 43 (4.65%) | |
| occurrences (all) | 12 | 2 | |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 6 / 44 (13.64%) | 2 / 43 (4.65%) | |
| occurrences (all) | 9 | 3 | |
| BACK PAIN | | | |
| subjects affected / exposed | 5 / 44 (11.36%) | 1 / 43 (2.33%) | |
| occurrences (all) | 5 | 2 | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 4 / 44 (9.09%) | 3 / 43 (6.98%) | |
| occurrences (all) | 6 | 3 | |
| NECK PAIN | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 1 / 43 (2.33%) | |
| occurrences (all) | 3 | 1 | |
| Infections and infestations | | | |
| UPPER RESPIRATORY TRACT INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 9 / 44 (20.45%) | 0 / 43 (0.00%) | |
| occurrences (all) | 15 | 0 | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 3 / 44 (6.82%) | 0 / 43 (0.00%) | |
| occurrences (all) | 3 | 0 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 05 December 2008 | Changes in inclusion and exclusion criteria. |
| 05 January 2010 | Rescue option for subjects who do not return to baseline after an accelerated switch described, changes in exclusion criteria, Data Monitoring Committee added, details of blinding/unblinded product added. |
| 01 March 2011 | Changes in inclusion criteria. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/11971045

http://www.ncbi.nlm.nih.gov/pubmed/10467380