



## Clinical trial results:

**Prospective 24-week, double-blind, randomized, placebo-controlled, multicenter study evaluating safety and change in efficacy-related surrogate parameters in patients with dementia of the Alzheimer's type under treatment with increasing dosages of intravenous immunoglobulin (octagam® 10%)**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2007-007134-19    |
| Trial protocol           | DE                |
| Global end of trial date | 21 September 2010 |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 04 January 2017 |
| First version publication date | 04 January 2017 |

### Trial information

#### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | GAM10-04 |
|-----------------------|----------|

#### Additional study identifiers

|                                    |                |
|------------------------------------|----------------|
| ISRCTN number                      | ISRCTN64846759 |
| ClinicalTrials.gov id (NCT number) | NCT00812565    |
| WHO universal trial number (UTN)   | -              |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Octapharma AG   |
| Sponsor organisation address | Seidenstrasse 2, Lachen, Switzerland, CH-8853   |
| Public contact               | Clinical Research and Development<br>Octapharma Pharmazeutica Produktionsgesellschaft m.b.H,<br>Octapharma Pharmazeutica Produktionsgesellschaft m.b.H,<br>+43 1 61032-0, |
| Scientific contact           | Clinical Research and Development<br>Octapharma Pharmazeutica Produktionsgesellschaft m.b.H,<br>Octapharma Pharmazeutica Produktionsgesellschaft m.b.H,<br>+43 1 61032-0, |

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                       | 27 November 2012  |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 21 September 2010 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to evaluate the decrease of A $\beta$  in the CNS and the increase in blood plasma, thereby corroborating the assumed primary mechanism of action of IVIG in AD patients, namely the interference with the pathomechanism for AD ("amyloid cascade hypothesis").

Protection of trial subjects:

This trial was conducted in accordance to the principles of GCP, ensuring that the rights, safety and well-being of patients are protected and in consistency with the Declaration of Helsinki. Inclusion and exclusion criteria were carefully defined in order to protect subjects from contraindications, interactions with other medication and risk factors associated with the investigational medicinal product. Throughout the study safety was assessed, such as occurrence of AEs, safety labs, vital signs and physical/neurological examinations, safety MRI.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 02 February 2009 |
| 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 | Germany: 18       |
| Country: Number of subjects enrolled | United States: 37 |
| Worldwide total number of subjects   | 55                |
| EEA total number of subjects         | 18                |

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)      | 14 |
| From 65 to 84 years       | 40 |
| 85 years and over         | 1  |

## Subject disposition

### Recruitment

Recruitment details:

The first patient was enrolled February 2, 2009. The last patient study visit was September 21, 2010. Patients were enrolled in this study from a variety of settings including private practice clinics and hospitals. There were 12 study sites, 5 in Germany and 7 in the United States.

### Pre-assignment

Screening details:

Qualified patients meeting all inclusion exclusion criteria and providing informed consent were enrolled into the trial.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Full Analyses Set              |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Investigator, Monitor, Subject |

### Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| <b>Arm title</b>             | Placebo Every 2 Weeks |

Arm description:

Participants received placebo intravenously every 2 weeks for 24 weeks (total of 12 infusions).

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

Dosage and administration details:

Participants received placebo intravenously every 2 weeks for 24 weeks (total of 12 infusions).

|                  |                                    |
|------------------|------------------------------------|
| <b>Arm title</b> | 0.1 g/kg Octagam 10% Every 2 Weeks |
|------------------|------------------------------------|

Arm description:

Participants received 0.1 g/kg Octagam 10% intravenously every 2 weeks for 24 weeks (total of 12 infusions).

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for infusion  |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

Participants received 0.1 g/kg octagam 10% intravenously every 2 weeks for 24 weeks (total of 12 infusions).

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | 0.25 g/kg Octagam 10% Every 2 Weeks |
|------------------|-------------------------------------|

Arm description:

Participants received 0.25 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).

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

|   |  |
|---|--|
| Investigational medicinal product name  | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for infusion  |
| Routes of administration  | Intravenous use  |
| Dosage and administration details:  |  |
| Participants received 0.25 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).             |  |
| <b>Arm title</b>  | 0.4 g/kg Octagam 10% Every 2 Weeks   |
| Arm description:  |  |
| Participants received of 0.4 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).           |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for infusion  |
| Routes of administration  | Intravenous use  |
| Dosage and administration details:  |  |
| Participants received of 0.4 g/kg octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).           |  |
| <b>Arm title</b>  | Placebo Every 4 Weeks  |
| Arm description:  |  |
| Participants received placebo intravenously every 4 weeks for 20 weeks (total of 6 infusions).              |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | Placebo  |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for infusion  |
| Routes of administration  | Intravenous use  |
| Dosage and administration details:  |  |
| Participants received placebo intravenously every 4 weeks for 20 weeks (total of 6 infusions).              |  |
| <b>Arm title</b>  | 0.2 g/kg Octagam 10% Every 4 Weeks   |
| Arm description:  |  |
| Participants received 0.2 g/kg octagam 10% intravenously every 4 weeks for 20 weeks (total of 6 infusions). |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for infusion  |
| Routes of administration  | Intravenous use  |
| Dosage and administration details:  |  |
| Participants received 0.2 g/kg octagam 10% intravenously every 4 weeks for 20 weeks (total of 6 infusions). |  |
| <b>Arm title</b>  | 0.5 g/kg Octagam 10% Every 4 Weeks   |
| Arm description:  |  |
| Participants received 0.5 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).               |  |
| Arm type  | Experimental   |

|  |  |
|--|--|
| Investigational medicinal product name | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for infusion  |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

Participants received 0.5 g/kg Octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).

|                  |                                    |
|------------------|------------------------------------|
| <b>Arm title</b> | 0.8 g/kg Octagam 10% Every 4 Weeks |
|------------------|------------------------------------|

Arm description:

Participants received of 0.8 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for infusion  |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

Participants received of 0.8 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).

| <b>Number of subjects in period 1</b> | Placebo Every 2 Weeks | 0.1 g/kg Octagam 10% Every 2 Weeks | 0.25 g/kg Octagam 10% Every 2 Weeks |
|---------------------------------------|-----------------------|------------------------------------|-------------------------------------|
| Started                               | 7                     | 6                                  | 7                                   |
| Completed                             | 7                     | 6                                  | 7                                   |

| <b>Number of subjects in period 1</b> | 0.4 g/kg Octagam 10% Every 2 Weeks | Placebo Every 4 Weeks | 0.2 g/kg Octagam 10% Every 4 Weeks |
|---------------------------------------|------------------------------------|-----------------------|------------------------------------|
| Started                               | 7                                  | 7                     | 6                                  |
| Completed                             | 7                                  | 7                     | 6                                  |

| <b>Number of subjects in period 1</b> | 0.5 g/kg Octagam 10% Every 4 Weeks | 0.8 g/kg Octagam 10% Every 4 Weeks |
|---------------------------------------|------------------------------------|------------------------------------|
| Started                               | 8                                  | 7                                  |
| Completed                             | 8                                  | 7                                  |

## Period 2

|                              |                                |
|------------------------------|--------------------------------|
| Period 2 title               | Completed                      |
| Is this the baseline period? | No                             |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Double blind                   |
| Roles blinded                | Subject, Investigator, Monitor |

**Arms**

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

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Placebo Every 2 Weeks |
|------------------|-----------------------|

## Arm description:

Participants received placebo intravenously every 2 weeks for 24 weeks (total of 12 infusions).

|          |         |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

|  |         |
|--|---------|
| Investigational medicinal product name | Placebo |
|--|---------|

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

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

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

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

## Dosage and administration details:

Participants received placebo intravenously every 2 weeks for 24 weeks (total of 12 infusions).

|                  |                                    |
|------------------|------------------------------------|
| <b>Arm title</b> | 0.1 g/kg Octagam 10% Every 2 Weeks |
|------------------|------------------------------------|

## Arm description:

Participants received 0.1 g/kg Octagam 10% intravenously every 2 weeks for 24 weeks (total of 12 infusions).

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

|  |  |
|--|--|
| Investigational medicinal product name | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
|--|--|

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

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

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

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

## Dosage and administration details:

Participants received 0.1 g/kg octagam 10% intravenously every 2 weeks for 24 weeks (total of 12 infusions).

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | 0.25 g/kg Octagam 10% Every 2 Weeks |
|------------------|-------------------------------------|

## Arm description:

Participants received 0.25 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).

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

|  |  |
|--|--|
| Investigational medicinal product name | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
|--|--|

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

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

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

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

## Dosage and administration details:

Participants received 0.25 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).

|                  |                                    |
|------------------|------------------------------------|
| <b>Arm title</b> | 0.4 g/kg Octagam 10% Every 2 Weeks |
|------------------|------------------------------------|

## Arm description:

Participants received of 0.4 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).

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

|  |  |
|--|--|
| Investigational medicinal product name | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
|--|--|

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

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

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

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

## Dosage and administration details:

Participants received of 0.4 g/kg octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).

|   |  |
|---|--|
| <b>Arm title</b>  | Placebo Every 4 Weeks  |
| Arm description:<br>Participants received placebo intravenously every 4 weeks for 20 weeks (total of 6 infusions).                                |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | Placebo  |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for infusion  |
| Routes of administration  | Intravenous use  |
| Dosage and administration details:<br>Participants received placebo intravenously every 4 weeks for 20 weeks (total of 6 infusions).              |  |
| <b>Arm title</b>  | 0.2 g/kg Octagam 10% Every 4 Weeks   |
| Arm description:<br>Participants received 0.2 g/kg octagam 10% intravenously every 4 weeks for 20 weeks (total of 6 infusions).                   |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for infusion  |
| Routes of administration  | Intravenous use  |
| Dosage and administration details:<br>Participants received 0.2 g/kg octagam 10% intravenously every 4 weeks for 20 weeks (total of 6 infusions). |  |
| <b>Arm title</b>  | 0.5 g/kg Octagam 10% Every 4 Weeks   |
| Arm description:<br>Participants received 0.5 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).                                 |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for infusion  |
| Routes of administration  | Intravenous use  |
| Dosage and administration details:<br>Participants received 0.5 g/kg Octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).               |  |
| <b>Arm title</b>  | 0.8 g/kg Octagam 10% Every 4 Weeks   |
| Arm description:<br>Participants received of 0.8 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).                              |  |
| Arm type  | Experimental   |
| Investigational medicinal product name  | Octagam 10%, human normal immunoglobulin solution ready for intravenous administration |
| Investigational medicinal product code  |  |
| Other name  |  |
| Pharmaceutical forms  | Solution for infusion  |
| Routes of administration  | Intravenous use  |
| Dosage and administration details:<br>Participants received of 0.8 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).            |  |



| <b>Number of subjects in period 2</b> | Placebo Every 2 Weeks | 0.1 g/kg Octagam 10% Every 2 Weeks | 0.25 g/kg Octagam 10% Every 2 Weeks |
|---------------------------------------|-----------------------|------------------------------------|-------------------------------------|
| Started                               | 7                     | 6                                  | 7                                   |
| Completed                             | 5                     | 6                                  | 7                                   |
| Not completed                         | 2                     | 0                                  | 0                                   |
| Consent withdrawn by subject          | 1                     | -                                  | -                                   |
| Adverse Event                         | -                     | -                                  | -                                   |
| Did Not Come To Study Visit           | 1                     | -                                  | -                                   |

| <b>Number of subjects in period 2</b> | 0.4 g/kg Octagam 10% Every 2 Weeks | Placebo Every 4 Weeks | 0.2 g/kg Octagam 10% Every 4 Weeks |
|---------------------------------------|------------------------------------|-----------------------|------------------------------------|
| Started                               | 7                                  | 7                     | 6                                  |
| Completed                             | 5                                  | 6                     | 6                                  |
| Not completed                         | 2                                  | 1                     | 0                                  |
| Consent withdrawn by subject          | -                                  | 1                     | -                                  |
| Adverse Event                         | 2                                  | -                     | -                                  |
| Did Not Come To Study Visit           | -                                  | -                     | -                                  |

| <b>Number of subjects in period 2</b> | 0.5 g/kg Octagam 10% Every 4 Weeks | 0.8 g/kg Octagam 10% Every 4 Weeks |
|---------------------------------------|------------------------------------|------------------------------------|
| Started                               | 8                                  | 7                                  |
| Completed                             | 8                                  | 6                                  |
| Not completed                         | 0                                  | 1                                  |
| Consent withdrawn by subject          | -                                  | -                                  |
| Adverse Event                         | -                                  | 1                                  |
| Did Not Come To Study Visit           | -                                  | -                                  |

## Baseline characteristics

### Reporting groups

|  |                                     |
|--|-------------------------------------|
| Reporting group title  | Placebo Every 2 Weeks               |
| Reporting group description:<br>Participants received placebo intravenously every 2 weeks for 24 weeks (total of 12 infusions).              |                                     |
| Reporting group title  | 0.1 g/kg Octagam 10% Every 2 Weeks  |
| Reporting group description:<br>Participants received 0.1 g/kg Octagam 10% intravenously every 2 weeks for 24 weeks (total of 12 infusions). |                                     |
| Reporting group title  | 0.25 g/kg Octagam 10% Every 2 Weeks |
| Reporting group description:<br>Participants received 0.25 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).              |                                     |
| Reporting group title  | 0.4 g/kg Octagam 10% Every 2 Weeks  |
| Reporting group description:<br>Participants received of 0.4 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).            |                                     |
| Reporting group title  | Placebo Every 4 Weeks               |
| Reporting group description:<br>Participants received placebo intravenously every 4 weeks for 20 weeks (total of 6 infusions).               |                                     |
| Reporting group title  | 0.2 g/kg Octagam 10% Every 4 Weeks  |
| Reporting group description:<br>Participants received 0.2 g/kg octagam 10% intravenously every 4 weeks for 20 weeks (total of 6 infusions).  |                                     |
| Reporting group title  | 0.5 g/kg Octagam 10% Every 4 Weeks  |
| Reporting group description:<br>Participants received 0.5 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).                |                                     |
| Reporting group title  | 0.8 g/kg Octagam 10% Every 4 Weeks  |
| Reporting group description:<br>Participants received of 0.8 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).             |                                     |

| Reporting group values                | Placebo Every 2 Weeks | 0.1 g/kg Octagam 10% Every 2 Weeks | 0.25 g/kg Octagam 10% Every 2 Weeks |
|---------------------------------------|-----------------------|------------------------------------|-------------------------------------|
| Number of subjects                    | 7                     | 6                                  | 7                                   |
| Age categorical<br>Units: Subjects    |                       |                                    |                                     |
| From 51-86 years                      | 7                     | 6                                  | 7                                   |
| Age continuous<br>Units: years        |                       |                                    |                                     |
| arithmetic mean                       | 72.57                 | 66.83                              | 68.29                               |
| standard deviation                    | ± 9.24                | ± 5.53                             | ± 4.15                              |
| Gender categorical<br>Units: Subjects |                       |                                    |                                     |
| Female                                | 4                     | 1                                  | 3                                   |
| Male                                  | 3                     | 5                                  | 4                                   |

| Reporting group values | 0.4 g/kg Octagam 10% Every 2 Weeks | Placebo Every 4 Weeks | 0.2 g/kg Octagam 10% Every 4 Weeks |
|------------------------|------------------------------------|-----------------------|------------------------------------|
| Number of subjects     | 7                                  | 7                     | 6                                  |

|                    |        |         |        |
|--------------------|--------|---------|--------|
| Age categorical    |        |         |        |
| Units: Subjects    |        |         |        |
| From 51-86 years   | 7      | 7       | 6      |
| Age continuous     |        |         |        |
| Units: years       |        |         |        |
| arithmetic mean    | 72.86  | 71.43   | 74.83  |
| standard deviation | ± 5.01 | ± 11.76 | ± 5.46 |
| Gender categorical |        |         |        |
| Units: Subjects    |        |         |        |
| Female             | 3      | 5       | 2      |
| Male               | 4      | 2       | 4      |

| <b>Reporting group values</b> | 0.5 g/kg Octagam<br>10% Every 4 Weeks | 0.8 g/kg Octagam<br>10% Every 4 Weeks | Total |
|-------------------------------|---------------------------------------|---------------------------------------|-------|
| Number of subjects            | 8                                     | 7                                     | 55    |
| Age categorical               |                                       |                                       |       |
| Units: Subjects               |                                       |                                       |       |
| From 51-86 years              | 8                                     | 7                                     | 55    |
| Age continuous                |                                       |                                       |       |
| Units: years                  |                                       |                                       |       |
| arithmetic mean               | 65.88                                 | 68.43                                 |       |
| standard deviation            | ± 10.19                               | ± 8.62                                | -     |
| Gender categorical            |                                       |                                       |       |
| Units: Subjects               |                                       |                                       |       |
| Female                        | 3                                     | 3                                     | 24    |
| Male                          | 5                                     | 4                                     | 31    |

## End points

### End points reporting groups

|  |                                     |
|--|-------------------------------------|
| Reporting group title  | Placebo Every 2 Weeks               |
| Reporting group description:<br>Participants received placebo intravenously every 2 weeks for 24 weeks (total of 12 infusions).              |                                     |
| Reporting group title  | 0.1 g/kg Octagam 10% Every 2 Weeks  |
| Reporting group description:<br>Participants received 0.1 g/kg Octagam 10% intravenously every 2 weeks for 24 weeks (total of 12 infusions). |                                     |
| Reporting group title  | 0.25 g/kg Octagam 10% Every 2 Weeks |
| Reporting group description:<br>Participants received 0.25 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).              |                                     |
| Reporting group title  | 0.4 g/kg Octagam 10% Every 2 Weeks  |
| Reporting group description:<br>Participants received of 0.4 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).            |                                     |
| Reporting group title  | Placebo Every 4 Weeks               |
| Reporting group description:<br>Participants received placebo intravenously every 4 weeks for 20 weeks (total of 6 infusions).               |                                     |
| Reporting group title  | 0.2 g/kg Octagam 10% Every 4 Weeks  |
| Reporting group description:<br>Participants received 0.2 g/kg octagam 10% intravenously every 4 weeks for 20 weeks (total of 6 infusions).  |                                     |
| Reporting group title  | 0.5 g/kg Octagam 10% Every 4 Weeks  |
| Reporting group description:<br>Participants received 0.5 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).                |                                     |
| Reporting group title  | 0.8 g/kg Octagam 10% Every 4 Weeks  |
| Reporting group description:<br>Participants received of 0.8 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).             |                                     |
| Reporting group title  | Placebo Every 2 Weeks               |
| Reporting group description:<br>Participants received placebo intravenously every 2 weeks for 24 weeks (total of 12 infusions).              |                                     |
| Reporting group title  | 0.1 g/kg Octagam 10% Every 2 Weeks  |
| Reporting group description:<br>Participants received 0.1 g/kg Octagam 10% intravenously every 2 weeks for 24 weeks (total of 12 infusions). |                                     |
| Reporting group title  | 0.25 g/kg Octagam 10% Every 2 Weeks |
| Reporting group description:<br>Participants received 0.25 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).              |                                     |
| Reporting group title  | 0.4 g/kg Octagam 10% Every 2 Weeks  |
| Reporting group description:<br>Participants received of 0.4 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).            |                                     |
| Reporting group title  | Placebo Every 4 Weeks               |
| Reporting group description:<br>Participants received placebo intravenously every 4 weeks for 20 weeks (total of 6 infusions).               |                                     |
| Reporting group title  | 0.2 g/kg Octagam 10% Every 4 Weeks  |
| Reporting group description:<br>Participants received 0.2 g/kg octagam 10% intravenously every 4 weeks for 20 weeks (total of 6 infusions).  |                                     |
| Reporting group title  | 0.5 g/kg Octagam 10% Every 4 Weeks  |
| Reporting group description:<br>Participants received 0.5 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).                |                                     |

|  |                                    |
|--|------------------------------------|
| Reporting group title  | 0.8 g/kg Octagam 10% Every 4 Weeks |
| Reporting group description:   |                                    |
| Participants received of 0.8 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions). |                                    |

**Primary: Change in the Area Under the Curve (AUC) of Plasma A $\beta$ 1-40 in the 2 or 4 weeks after the last treatment infusion from the trough level prior to the last treatment infusion**

|                 |   |
|-----------------|---|
| End point title | Change in the Area Under the Curve (AUC) of Plasma A $\beta$ 1-40 in the 2 or 4 weeks after the last treatment infusion from the trough level prior to the last treatment infusion <sup>[1]</sup> |
|-----------------|---|

End point description:

For participants who received infusions every 2 weeks, plasma samples were collected at the trough level at Week 22 and on Days 1, 4, 7, and 14 after Week 22. For participants who received infusions every 4 weeks, plasma samples were collected at the trough level at Week 20 and on Days 1, 4, 7, 14, 21, and 28 after Week 20. Samples for determining A $\beta$ 1-40 in blood plasma were processed at a central laboratory using a commercially available kit from Innogenetics NV (INNO-BIA plasma A $\beta$  forms; Gent, Belgium).

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

End point timeframe:

Week 22 to Week 24 for participants who received infusions every 2 weeks and Week 20 to Week 24 participants who received infusions every 4 weeks

Notes:

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

Justification: Results are provided as Change in the Area Under the Curve of Plasma A $\beta$ 1-40 in the 2 or 4 Weeks After the Last Treatment Infusion From the Trough Level Prior to the Last Treatment Infusion

| End point values                     | Placebo Every 2 Weeks | 0.1 g/kg Octagam 10% Every 2 Weeks | 0.25 g/kg Octagam 10% Every 2 Weeks | 0.4 g/kg Octagam 10% Every 2 Weeks |
|--------------------------------------|-----------------------|------------------------------------|-------------------------------------|------------------------------------|
| Subject group type                   | Reporting group       | Reporting group                    | Reporting group                     | Reporting group                    |
| Number of subjects analysed          | 5                     | 6                                  | 7                                   | 5                                  |
| Units: (pg/mL)*days]                 |                       |                                    |                                     |                                    |
| arithmetic mean (standard deviation) | 161.2 ( $\pm$ 93.9)   | -245.67 ( $\pm$ 747.58)            | -122.5 ( $\pm$ 478.31)              | -39.1 ( $\pm$ 172.72)              |

| End point values                     | Placebo Every 4 Weeks  | 0.2 g/kg Octagam 10% Every 4 Weeks | 0.5 g/kg Octagam 10% Every 4 Weeks | 0.8 g/kg Octagam 10% Every 4 Weeks |
|--------------------------------------|------------------------|------------------------------------|------------------------------------|------------------------------------|
| Subject group type                   | Reporting group        | Reporting group                    | Reporting group                    | Reporting group                    |
| Number of subjects analysed          | 6                      | 6                                  | 8                                  | 6                                  |
| Units: (pg/mL)*days]                 |                        |                                    |                                    |                                    |
| arithmetic mean (standard deviation) | 510.92 ( $\pm$ 2395.8) | -83.67 ( $\pm$ 957.69)             | -755.38 ( $\pm$ 2232.87)           | -262.92 ( $\pm$ 671.37)            |

**Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were monitored throughout the entire study period, starting from the baseline visit until the final study visit.

Adverse event reporting additional description:

Safety set: All randomized participants who received at least 1 infusion of study medication

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Placebo Every 2 Weeks |
|-----------------------|-----------------------|

Reporting group description:

Participants received placebo intravenously every 2 weeks for 24 weeks (total of 12 infusions).

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | 0.1 g/kg Octagam 10% Every 2 Weeks |
|-----------------------|------------------------------------|

Reporting group description:

Participants received 0.1 g/kg Octagam 10% intravenously every 2 weeks for 24 weeks (total of 12 infusions).

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | 0.25 g/kg Octagam 10% Every 2 Weeks |
|-----------------------|-------------------------------------|

Reporting group description:

Participants received 0.25 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | 0.4 g/kg Octagam 10% Every 2 Weeks |
|-----------------------|------------------------------------|

Reporting group description:

Participants received of 0.4 g/kg Octagam 10% every 2 weeks for 24 weeks (total of 12 infusions).

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Placebo Every 4 Weeks |
|-----------------------|-----------------------|

Reporting group description:

Participants received placebo intravenously every 4 weeks for 20 weeks (total of 6 infusions).

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | 0.2 g/kg Octagam 10% Every 4 Weeks |
|-----------------------|------------------------------------|

Reporting group description:

Participants received 0.2 g/kg octagam 10% intravenously every 4 weeks for 20 weeks (total of 6 infusions).

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | 0.5 g/kg Octagam 10% Every 4 Weeks |
|-----------------------|------------------------------------|

Reporting group description:

Participants received 0.5 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | 0.8 g/kg Octagam 10% Every 4 Weeks |
|-----------------------|------------------------------------|

Reporting group description:

Participants received of 0.8 g/kg octagam 10% every 4 weeks for 20 weeks (total of 6 infusions).

| Serious adverse events                            | Placebo Every 2 Weeks | 0.1 g/kg Octagam 10% Every 2 Weeks | 0.25 g/kg Octagam 10% Every 2 Weeks |
|---|-----------------------|------------------------------------|-------------------------------------|
| Total subjects affected by serious adverse events |                       |                                    |                                     |
| subjects affected / exposed                       | 2 / 7 (28.57%)        | 1 / 6 (16.67%)                     | 0 / 7 (0.00%)                       |
| number of deaths (all causes)                     | 0                     | 0                                  | 0                                   |
| number of deaths resulting from adverse events    | 0                     | 0                                  | 0                                   |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Surgical and medical procedures                 |                |                |               |
| Knee arthroplasty                               |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Spinal laminectomy                              |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Nervous system disorders                        |                |                |               |
| Cerebral infarction                             |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Convulsion                                      |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Dementia Alzheimer's type                       |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Gastrointestinal disorders                      |                |                |               |
| Gastric antral vascular ectasia                 |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Nausea  |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Vomiting  |                |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Psychiatric disorders                           |               |                |               |
| Delirium  |               |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Aggression                                      |               |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |

| Serious adverse events                            | 0.4 g/kg Octagam<br>10% Every 2 Weeks | Placebo Every 4<br>Weeks | 0.2 g/kg Octagam<br>10% Every 4 Weeks |
|---|---------------------------------------|--------------------------|---------------------------------------|
| Total subjects affected by serious adverse events |                                       |                          |                                       |
| subjects affected / exposed                       | 2 / 7 (28.57%)                        | 2 / 7 (28.57%)           | 0 / 7 (0.00%)                         |
| number of deaths (all causes)                     | 0                                     | 0                        | 0                                     |
| number of deaths resulting from adverse events    | 0                                     | 0                        | 0                                     |
| Surgical and medical procedures                   |                                       |                          |                                       |
| Knee arthroplasty                                 |                                       |                          |                                       |
| subjects affected / exposed                       | 0 / 7 (0.00%)                         | 0 / 7 (0.00%)            | 0 / 7 (0.00%)                         |
| occurrences causally related to treatment / all   | 0 / 0                                 | 0 / 0                    | 0 / 0                                 |
| deaths causally related to treatment / all        | 0 / 0                                 | 0 / 0                    | 0 / 0                                 |
| Spinal laminectomy                                |                                       |                          |                                       |
| subjects affected / exposed                       | 0 / 7 (0.00%)                         | 0 / 7 (0.00%)            | 0 / 7 (0.00%)                         |
| occurrences causally related to treatment / all   | 0 / 0                                 | 0 / 0                    | 0 / 0                                 |
| deaths causally related to treatment / all        | 0 / 0                                 | 0 / 0                    | 0 / 0                                 |
| Nervous system disorders                          |                                       |                          |                                       |
| Cerebral infarction                               |                                       |                          |                                       |
| subjects affected / exposed                       | 1 / 7 (14.29%)                        | 0 / 7 (0.00%)            | 0 / 7 (0.00%)                         |
| occurrences causally related to treatment / all   | 0 / 1                                 | 0 / 0                    | 0 / 0                                 |
| deaths causally related to treatment / all        | 0 / 0                                 | 0 / 0                    | 0 / 0                                 |
| Convulsion  |                                       |                          |                                       |



|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Dementia Alzheimer's type                       |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Gastrointestinal disorders                      |                |                |               |
| Gastric antral vascular ectasia                 |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Nausea  |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Vomiting  |                |                |               |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Psychiatric disorders                           |                |                |               |
| Delirium  |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Aggression                                      |                |                |               |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 7 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |

| <b>Serious adverse events</b>                     | 0.5 g/kg Octagam<br>10% Every 4 Weeks | 0.8 g/kg Octagam<br>10% Every 4 Weeks |  |
|---|---------------------------------------|---------------------------------------|--|
| Total subjects affected by serious adverse events |                                       |                                       |  |
| subjects affected / exposed                       | 1 / 8 (12.50%)                        | 0 / 7 (0.00%)                         |  |
| number of deaths (all causes)                     | 0                                     | 0                                     |  |
| number of deaths resulting from                   | 0                                     | 0                                     |  |

|   |                |               |  |
|---|----------------|---------------|--|
| adverse events                                  |                |               |  |
| Surgical and medical procedures                 |                |               |  |
| Knee arthroplasty                               |                |               |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Spinal laminectomy                              |                |               |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Nervous system disorders                        |                |               |  |
| Cerebral infarction                             |                |               |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Convulsion                                      |                |               |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Dementia Alzheimer's type                       |                |               |  |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Gastrointestinal disorders                      |                |               |  |
| Gastric antral vascular ectasia                 |                |               |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Nausea  |                |               |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Vomiting  |                |               |  |

|   |               |               |  |
|---|---------------|---------------|--|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Psychiatric disorders                           |               |               |  |
| Delirium  |               |               |  |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |
| Aggression                                      |               |               |  |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 7 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         |  |

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

| <b>Non-serious adverse events</b>                     | Placebo Every 2 Weeks | 0.1 g/kg Octagam 10% Every 2 Weeks | 0.25 g/kg Octagam 10% Every 2 Weeks |
|---|-----------------------|------------------------------------|-------------------------------------|
| Total subjects affected by non-serious adverse events |                       |                                    |                                     |
| subjects affected / exposed                           | 5 / 7 (71.43%)        | 4 / 6 (66.67%)                     | 5 / 7 (71.43%)                      |
| Vascular disorders                                    |                       |                                    |                                     |
| Blood pressure fluctuation                            |                       |                                    |                                     |
| subjects affected / exposed                           | 0 / 7 (0.00%)         | 0 / 6 (0.00%)                      | 1 / 7 (14.29%)                      |
| occurrences (all)                                     | 0                     | 0                                  | 2                                   |
| Hypertension  |                       |                                    |                                     |
| subjects affected / exposed                           | 0 / 7 (0.00%)         | 0 / 6 (0.00%)                      | 0 / 7 (0.00%)                       |
| occurrences (all)                                     | 0                     | 0                                  | 0                                   |
| Hypotension   |                       |                                    |                                     |
| subjects affected / exposed                           | 1 / 7 (14.29%)        | 0 / 6 (0.00%)                      | 0 / 7 (0.00%)                       |
| occurrences (all)                                     | 1                     | 0                                  | 0                                   |
| Vasoconstriction                                      |                       |                                    |                                     |
| subjects affected / exposed                           | 0 / 7 (0.00%)         | 0 / 6 (0.00%)                      | 0 / 7 (0.00%)                       |
| occurrences (all)                                     | 0                     | 0                                  | 0                                   |
| General disorders and administration site conditions  |                       |                                    |                                     |
| Chills  |                       |                                    |                                     |
| subjects affected / exposed                           | 0 / 7 (0.00%)         | 0 / 6 (0.00%)                      | 1 / 7 (14.29%)                      |
| occurrences (all)                                     | 0                     | 0                                  | 1                                   |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Fatigue   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Influenza like illness                          |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 2 / 7 (28.57%) |
| occurrences (all)                               | 0             | 0              | 2              |
| Infusion site extravasation                     |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Pyrexia   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Submandibular mass                              |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |               |                |                |
| Respiratory tract congestion                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Rhinorrhoea                                     |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Psychiatric disorders                           |               |                |                |
| Agitation                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Confusional state                               |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Depression                                      |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Insomnia  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Investigations                                  |               |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Aspartate aminotransferase increased           |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Blood creatine phosphokinase increased         |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0              |
| Blood iron decreased                           |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Blood lactate dehydrogenase increased          |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Blood magnesium decreased                      |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Blood potassium decreased                      |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Blood pressure decreased                       |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                              | 0              | 0              | 1              |
| CSF white blood cell count positive            |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0              |
| Weight decreased                               |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Anxiety postoperative                          |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0              |
| Contusion                                      |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                              | 0              | 0              | 1              |

|                               |                |                |                |
|-------------------------------|----------------|----------------|----------------|
| Fall                          |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)             | 0              | 0              | 2              |
| Periorbital haematoma         |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)             | 0              | 0              | 1              |
| Post lumbar puncture syndrome |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0              |
| Post procedural constipation  |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0              |
| Post procedural haemorrhage   |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0              |
| Procedural headache           |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0              |
| Procedural hypertension       |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0              |
| Procedural pain               |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0              |
| Cardiac disorders             |                |                |                |
| Atrial fibrillation           |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0              |
| Nervous system disorders      |                |                |                |
| Cerebral haemorrhage          |                |                |                |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 2 / 6 (33.33%) | 1 / 7 (14.29%) |
| occurrences (all)             | 0              | 2              | 1              |
| Dizziness                     |                |                |                |
| subjects affected / exposed   | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0              |
| Essential tremor              |                |                |                |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Headache                             |                |                |                |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                    | 1              | 0              | 2              |
| Hypertonia                           |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Hypoaesthesia                        |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Hyporeflexia                         |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 6 (16.67%) | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Paraesthesia                         |                |                |                |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Tremor                               |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Blood and lymphatic system disorders |                |                |                |
| Anaemia                              |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Iron deficiency anaemia              |                |                |                |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Lymphadenopathy                      |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Ear and labyrinth disorders          |                |                |                |
| Hearing impaired                     |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 6 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Eye disorders                        |                |                |                |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| Glaucoma<br>subjects affected / exposed<br>occurrences (all)              | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Gastrointestinal disorders  |                     |                     |                     |
| Colitis microscopic<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Colonic polyp<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 7 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 7 (0.00%)<br>0  |
| Gastrointestinal pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Hiatus hernia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)              | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders                                    |                     |                     |                     |
| Actinic keratosis<br>subjects affected / exposed<br>occurrences (all)     | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)    | 0 / 7 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 7 (0.00%)<br>0  |
| Ecchymosis<br>subjects affected / exposed<br>occurrences (all)            | 1 / 7 (14.29%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Hyperkeratosis<br>subjects affected / exposed<br>occurrences (all)        | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Pruritus  |                     |                     |                     |



|   |                    |                     |                     |
|---|--------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Renal and urinary disorders<br>Haematuria<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 7 (14.29%)<br>2 |
| Rotator cuff syndrome<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 | 0 / 7 (0.00%)<br>0  |
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 7 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |

| <b>Non-serious adverse events</b>                           | <b>0.4 g/kg Octagam<br/>10% Every 2 Weeks</b> | <b>Placebo Every 4<br/>Weeks</b> | <b>0.2 g/kg Octagam<br/>10% Every 4 Weeks</b> |
|---|---|----------------------------------|---|
| Total subjects affected by non-serious adverse events       |   |                                  |   |
| subjects affected / exposed                                 | 3 / 7 (42.86%)                                | 3 / 7 (42.86%)                   | 4 / 7 (57.14%)                                |
| <b>Vascular disorders</b>                                   |   |                                  |   |
| Blood pressure fluctuation                                  |   |                                  |   |
| subjects affected / exposed                                 | 0 / 7 (0.00%)                                 | 0 / 7 (0.00%)                    | 0 / 7 (0.00%)                                 |
| occurrences (all)   | 0   | 0                                | 0   |
| Hypertension  |   |                                  |   |
| subjects affected / exposed                                 | 0 / 7 (0.00%)                                 | 0 / 7 (0.00%)                    | 0 / 7 (0.00%)                                 |
| occurrences (all)   | 0   | 0                                | 0   |
| Hypotension   |   |                                  |   |
| subjects affected / exposed                                 | 0 / 7 (0.00%)                                 | 0 / 7 (0.00%)                    | 0 / 7 (0.00%)                                 |
| occurrences (all)   | 0   | 0                                | 0   |
| Vasoconstriction  |   |                                  |   |
| subjects affected / exposed                                 | 1 / 7 (14.29%)                                | 0 / 7 (0.00%)                    | 0 / 7 (0.00%)                                 |
| occurrences (all)   | 1   | 0                                | 0   |
| <b>General disorders and administration site conditions</b> |   |                                  |   |
| Chills  |   |                                  |   |
| subjects affected / exposed                                 | 0 / 7 (0.00%)                                 | 0 / 7 (0.00%)                    | 0 / 7 (0.00%)                                 |
| occurrences (all)   | 0   | 0                                | 0   |
| Fatigue   |   |                                  |   |
| subjects affected / exposed                                 | 0 / 7 (0.00%)                                 | 0 / 7 (0.00%)                    | 0 / 7 (0.00%)                                 |
| occurrences (all)   | 0   | 0                                | 0   |
| Influenza like illness                                      |   |                                  |   |
| subjects affected / exposed                                 | 0 / 7 (0.00%)                                 | 0 / 7 (0.00%)                    | 0 / 7 (0.00%)                                 |
| occurrences (all)   | 0   | 0                                | 0   |
| Infusion site extravasation                                 |   |                                  |   |
| subjects affected / exposed                                 | 0 / 7 (0.00%)                                 | 0 / 7 (0.00%)                    | 1 / 7 (14.29%)                                |
| occurrences (all)   | 0   | 0                                | 2   |
| Pyrexia   |   |                                  |   |
| subjects affected / exposed                                 | 0 / 7 (0.00%)                                 | 0 / 7 (0.00%)                    | 0 / 7 (0.00%)                                 |
| occurrences (all)   | 0   | 0                                | 0   |
| Submandibular mass  |   |                                  |   |
| subjects affected / exposed                                 | 0 / 7 (0.00%)                                 | 0 / 7 (0.00%)                    | 0 / 7 (0.00%)                                 |
| occurrences (all)   | 0   | 0                                | 0   |
| <b>Respiratory, thoracic and mediastinal disorders</b>      |   |                                  |   |

|   |                    |                     |                     |
|---|--------------------|---------------------|---------------------|
| Respiratory tract congestion<br>subjects affected / exposed<br>occurrences (all)              | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Psychiatric disorders   |                    |                     |                     |
| Agitation<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 7 (0.00%)<br>0 | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0  |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |
| Depression<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Investigations  |                    |                     |                     |
| Aspartate aminotransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Blood creatine phosphokinase<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Blood iron decreased<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 7 (0.00%)<br>0 | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0  |
| Blood lactate dehydrogenase<br>increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  |
| Blood magnesium decreased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 7 (0.00%)<br>0 | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0  |

|   |                     |                     |                    |
|---|---------------------|---------------------|--------------------|
| Blood potassium decreased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 7 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0 |
| Blood pressure decreased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| CSF white blood cell count positive<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Injury, poisoning and procedural complications  |                     |                     |                    |
| Anxiety postoperative<br>subjects affected / exposed<br>occurrences (all)               | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Periorbital haematoma<br>subjects affected / exposed<br>occurrences (all)               | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Post lumbar puncture syndrome<br>subjects affected / exposed<br>occurrences (all)       | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Post procedural constipation<br>subjects affected / exposed<br>occurrences (all)        | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Post procedural haemorrhage<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Procedural headache   |                     |                     |                    |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Procedural hypertension     |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Procedural pain             |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Cardiac disorders           |               |                |                |
| Atrial fibrillation         |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Nervous system disorders    |               |                |                |
| Cerebral haemorrhage        |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Dizziness                   |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Essential tremor            |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Headache                    |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)           | 0             | 0              | 1              |
| Hypertonia                  |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hypoaesthesia               |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Hyporeflexia                |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Paraesthesia                |               |                |                |

|   |                    |                     |                    |
|---|--------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Tremor<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Iron deficiency anaemia<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Ear and labyrinth disorders<br>Hearing impaired<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Eye disorders<br>Glaucoma<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Gastrointestinal disorders<br>Colitis microscopic<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0 | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0 |
| Colonic polyp<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 7 (0.00%)<br>0 | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0 |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Gastrointestinal pain<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 7 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 |
| Hiatus hernia   |                    |                     |                    |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Vomiting  |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Actinic keratosis                               |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Dermatitis contact                              |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Ecchymosis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Hyperkeratosis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Pruritus  |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Renal and urinary disorders                     |                |                |                |
| Haematuria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Muscle spasms                                   |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Rotator cuff syndrome                           |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Infections and infestations                     |                |                |                |

|                                   |               |                |                |
|-----------------------------------|---------------|----------------|----------------|
| Bronchitis                        |               |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 1 / 7 (14.29%) |
| occurrences (all)                 | 0             | 0              | 1              |
| Gastroenteritis                   |               |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Tooth abscess                     |               |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Tooth infection                   |               |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |
| Upper respiratory tract infection |               |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%) | 1 / 7 (14.29%) | 0 / 7 (0.00%)  |
| occurrences (all)                 | 0             | 1              | 0              |
| Urinary tract infection           |               |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0              |

| <b>Non-serious adverse events</b>                     | 0.5 g/kg Octagam<br>10% Every 4 Weeks | 0.8 g/kg Octagam<br>10% Every 4 Weeks |  |
|---|---------------------------------------|---------------------------------------|--|
| Total subjects affected by non-serious adverse events |                                       |                                       |  |
| subjects affected / exposed                           | 4 / 8 (50.00%)                        | 4 / 7 (57.14%)                        |  |
| Vascular disorders                                    |                                       |                                       |  |
| Blood pressure fluctuation                            |                                       |                                       |  |
| subjects affected / exposed                           | 0 / 8 (0.00%)                         | 0 / 7 (0.00%)                         |  |
| occurrences (all)                                     | 0                                     | 0                                     |  |
| Hypertension  |                                       |                                       |  |
| subjects affected / exposed                           | 0 / 8 (0.00%)                         | 1 / 7 (14.29%)                        |  |
| occurrences (all)                                     | 0                                     | 1                                     |  |
| Hypotension   |                                       |                                       |  |
| subjects affected / exposed                           | 0 / 8 (0.00%)                         | 0 / 7 (0.00%)                         |  |
| occurrences (all)                                     | 0                                     | 0                                     |  |
| Vasoconstriction                                      |                                       |                                       |  |
| subjects affected / exposed                           | 0 / 8 (0.00%)                         | 0 / 7 (0.00%)                         |  |
| occurrences (all)                                     | 0                                     | 0                                     |  |
| General disorders and administration site conditions  |                                       |                                       |  |



|   |                |                |  |
|---|----------------|----------------|--|
| Chills  |                |                |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 0              | 0              |  |
| Fatigue   |                |                |  |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Influenza like illness                          |                |                |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 0              | 0              |  |
| Infusion site extravasation                     |                |                |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 0              | 0              |  |
| Pyrexia   |                |                |  |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Submandibular mass                              |                |                |  |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Respiratory tract congestion                    |                |                |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 0              | 0              |  |
| Rhinorrhoea                                     |                |                |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 0              | 0              |  |
| Psychiatric disorders                           |                |                |  |
| Agitation                                       |                |                |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 0              | 0              |  |
| Confusional state                               |                |                |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                               | 0              | 0              |  |
| Depression                                      |                |                |  |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Insomnia  |                |                |  |

|  |               |                |  |
|--|---------------|----------------|--|
| subjects affected / exposed                    | 0 / 8 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)                              | 0             | 1              |  |
| Investigations                                 |               |                |  |
| Aspartate aminotransferase increased           |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)                              | 0             | 1              |  |
| Blood creatine phosphokinase increased         |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                              | 0             | 0              |  |
| Blood iron decreased                           |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                              | 0             | 0              |  |
| Blood lactate dehydrogenase increased          |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)                              | 0             | 1              |  |
| Blood magnesium decreased                      |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                              | 0             | 0              |  |
| Blood potassium decreased                      |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                              | 0             | 0              |  |
| Blood pressure decreased                       |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                              | 0             | 0              |  |
| CSF white blood cell count positive            |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                              | 0             | 0              |  |
| Weight decreased                               |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)                              | 0             | 1              |  |
| Injury, poisoning and procedural complications |               |                |  |
| Anxiety postoperative                          |               |                |  |
| subjects affected / exposed                    | 0 / 8 (0.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                              | 0             | 0              |  |

|                               |                |                |  |
|-------------------------------|----------------|----------------|--|
| Contusion                     |                |                |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 0              | 0              |  |
| Fall                          |                |                |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 1              | 0              |  |
| Periorbital haematoma         |                |                |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 0              | 0              |  |
| Post lumbar puncture syndrome |                |                |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 0              | 0              |  |
| Post procedural constipation  |                |                |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 0              | 0              |  |
| Post procedural haemorrhage   |                |                |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 0              | 0              |  |
| Procedural headache           |                |                |  |
| subjects affected / exposed   | 1 / 8 (12.50%) | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 1              | 0              |  |
| Procedural hypertension       |                |                |  |
| subjects affected / exposed   | 1 / 8 (12.50%) | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 1              | 0              |  |
| Procedural pain               |                |                |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 0              | 0              |  |
| Cardiac disorders             |                |                |  |
| Atrial fibrillation           |                |                |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)             | 0              | 0              |  |
| Nervous system disorders      |                |                |  |
| Cerebral haemorrhage          |                |                |  |
| subjects affected / exposed   | 1 / 8 (12.50%) | 1 / 7 (14.29%) |  |
| occurrences (all)             | 1              | 1              |  |
| Dizziness                     |                |                |  |

|                                      |                |                |  |
|--------------------------------------|----------------|----------------|--|
| subjects affected / exposed          | 0 / 8 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Essential tremor                     |                |                |  |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Headache                             |                |                |  |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 1              | 0              |  |
| Hypertonia                           |                |                |  |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 0              | 0              |  |
| Hypoaesthesia                        |                |                |  |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 1              | 0              |  |
| Hyporeflexia                         |                |                |  |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 0              | 0              |  |
| Paraesthesia                         |                |                |  |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 0              | 0              |  |
| Tremor                               |                |                |  |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 0              | 0              |  |
| Blood and lymphatic system disorders |                |                |  |
| Anaemia                              |                |                |  |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 0              | 0              |  |
| Iron deficiency anaemia              |                |                |  |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 0              | 0              |  |
| Lymphadenopathy                      |                |                |  |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 1              | 0              |  |
| Ear and labyrinth disorders          |                |                |  |
| Hearing impaired                     |                |                |  |

|  |                    |                     |  |
|--|--------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Eye disorders                                    |                    |                     |  |
| Glaucoma   |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 1 / 7 (14.29%)<br>1 |  |
| Gastrointestinal disorders                       |                    |                     |  |
| Colitis microscopic                              |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Colonic polyp                                    |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Dyspepsia  |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Gastrointestinal pain                            |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Hiatus hernia                                    |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Vomiting   |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Skin and subcutaneous tissue disorders           |                    |                     |  |
| Actinic keratosis                                |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Dermatitis contact                               |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Ecchymosis                                       |                    |                     |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Hyperkeratosis                                   |                    |                     |  |

|   |                    |                     |  |
|---|--------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Renal and urinary disorders<br>Haematuria<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Rotator cuff syndrome<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0 | 1 / 7 (14.29%)<br>1 |  |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 8 (0.00%)<br>0 | 0 / 7 (0.00%)<br>0  |  |
| Urinary tract infection   |                    |                     |  |

|                             |               |                |  |
|-----------------------------|---------------|----------------|--|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 1              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 10 June 2009    | Amendment 1 (global, dated 10 June 2009): The changes were a result of issues encountered during the initial conduct of the trial that identified protocol requirements that were impractical and/or unnecessary for the study conduct. Other changes were administrative corrections or clarification of existing language. The specified changes referred to numbers of sites per country, time windows, sample collection and laboratory procedures and to the procedure of obtaining informed consent. |
| 07 October 2009 | Some mistakes/inconsistencies made in protocol version 2.3 were corrected. The specified changes referred to the numbers of sites per country and time windows.  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

|  |
|--|
| Small numbers of patients per treatment group (between 5 and 8) and variable total A $\beta$ levels over time. |
|--|

Notes: