



## Clinical trial results: Post-Authorization Safety, Tolerability and Immunogenicity Evaluation of HyQvia in Pediatric Subjects With Primary Immunodeficiency Diseases

### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2016-003438-26          |
| Trial protocol           | GB SE DK CZ SK FR GR HU |
| Global end of trial date | 15 January 2021         |

### Results information

|                                |                                                                                                                                            |
|--------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| Result version number          | v2 (current)                                                                                                                               |
| This version publication date  | 30 April 2022                                                                                                                              |
| First version publication date | 04 August 2021                                                                                                                             |
| Version creation reason        | <ul style="list-style-type: none"><li>• New data added to full data set</li></ul> Study results data have been updated based on final CSR. |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 161504 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03116347 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                              |
|------------------------------|------------------------------------------------------------------------------|
| Sponsor organisation name    | Baxalta Innovations GmbH                                                     |
| Sponsor organisation address | Industriestrasse 67, Vienna, Austria, 1220                                   |
| Public contact               | Study Director, Baxalta Innovations GmbH,<br>ClinicalTransparency@takeda.com |
| Scientific contact           | Study Director, Baxalta Innovations GmbH,<br>ClinicalTransparency@takeda.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                 |
|------------------------------------------------------|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 15 January 2021 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 15 January 2021 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the safety of HyQvia treatment in pediatric subjects with Primary Immunodeficiency Diseases (PIDD) who received immunoglobulin therapy prior to study enrollment.

Protection of trial subjects:

This study was conducted in accordance with the principles and guidelines described in the study protocol, the International Council for Harmonisation Guideline for Good Clinical Practice E6 (ICH GCP R2, November 2016), Title 21 of the United States (US) Code of Federal Regulations, the European Union (EU) Directives 2001/20/EC and 2005/28/EC, the Declaration of Helsinki, and applicable national and local regulatory requirements.

Background therapy: -

Evidence for comparator: -

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 30 May 2017 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | No          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Czechia: 7        |
| Country: Number of subjects enrolled | Denmark: 3        |
| Country: Number of subjects enrolled | France: 1         |
| Country: Number of subjects enrolled | Greece: 6         |
| Country: Number of subjects enrolled | Slovakia: 9       |
| Country: Number of subjects enrolled | Sweden: 4         |
| Country: Number of subjects enrolled | United Kingdom: 9 |
| Country: Number of subjects enrolled | Hungary: 3        |
| Worldwide total number of subjects   | 42                |
| EEA total number of subjects         | 33                |

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)                    | 21 |
| Adolescents (12-17 years)                | 21 |
| Adults (18-64 years)                     | 0  |
| From 65 to 84 years                      | 0  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 42 subjects were enrolled and treated. This study consisted of 3 treatment periods: Epoch 1 (E1), Epoch 2 (E2) and Epoch 3 (E3). Subject with anti-rHuPH20 antibody titer  $\geq 160$  during E1 or E2 and who experienced either a related serious or severe adverse event (AE) was followed to E3.

### Pre-assignment

Screening details:

Subjects treated with HyQvia in E1 followed by E2 were referred as "HyQvia new starters" and who started directly in E2 were referred as "HyQvia pre-treated". 1 subject from "HyQvia new starters" discontinued E2, entered E3 due to a severe related AE and didn't receive HyQvia treatment in E3. No further safety and efficacy data were collected in E3

### Period 1

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

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | HyQvia New Starters |

Arm description:

Subjects who were treated with non-HyQvia treatment by time of enrollment were enrolled in Epoch 1 (ramp-up) and treated with HyQvia subcutaneously (SC) with a dose or interval ramp-up period of up to 6 weeks. HyQvia dose was planned to be equivalent to 100% ( $\pm 5\%$ ) of pre-study treatment. Dosage frequency was one treatment interval of one week, then one treatment interval of two weeks, then one treatment interval of three weeks (for subjects in whom treatment was expected to be every four weeks). The ramp-up period was followed by Epoch 2 with HyQvia SC treatment at every 3 or 4 weeks, depending on the subject's previous dosing schedule and the discretion of the investigator and subject, for up to 20 months.

|                                        |                                                                          |
|----------------------------------------|--------------------------------------------------------------------------|
| Arm type                               | Experimental                                                             |
| Investigational medicinal product name | 10% (Human) with Recombinant Human Hyaluronidase (IGI, 10% with rHuPH20) |
| Investigational medicinal product code |                                                                          |
| Other name                             | HyQvia                                                                   |
| Pharmaceutical forms                   | Solution for infusion                                                    |
| Routes of administration               | Subcutaneous use                                                         |

Dosage and administration details:

Subjects treated with HyQvia subcutaneously with a dose or interval ramp-up period of up to 6 weeks in Epoch 1.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | HyQvia Pre-treated |
|------------------|--------------------|

Arm description:

Subjects already treated with HYQVIA by the time of enrollment were directly enrolled in Epoch 2 and treated with HyQvia SC at every 3 or 4 weeks for up to 20 months. HyQvia dose was planned to be equivalent to 100% ( $\pm 5\%$ ) of pre-study treatment with a dosage frequency of once every three or four weeks, based on the subject's previous dosing schedule and the discretion of the investigator and subject.

|                                        |                                                                          |
|----------------------------------------|--------------------------------------------------------------------------|
| Arm type                               | Experimental                                                             |
| Investigational medicinal product name | 10% (Human) with Recombinant Human Hyaluronidase (IGI, 10% with rHuPH20) |
| Investigational medicinal product code |                                                                          |
| Other name                             | HyQvia                                                                   |
| Pharmaceutical forms                   | Solution for infusion                                                    |
| Routes of administration               | Subcutaneous use                                                         |

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**Dosage and administration details:**

Subjects already treated with HYQVIA by the time of enrollment were directly enrolled in Epoch 2 and treated with HyQvia SC at every 3 or 4 weeks for up to 20 months.

| <b>Number of subjects in period 1</b> | HyQvia New Starters | HyQvia Pre-treated |
|---------------------------------------|---------------------|--------------------|
| Started                               | 23                  | 19                 |
| Completed                             | 22                  | 17                 |
| Not completed                         | 1                   | 2                  |
| Consent withdrawn by subject          | 1                   | 2                  |

## Baseline characteristics

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | HyQvia New Starters |
|-----------------------|---------------------|

Reporting group description:

Subjects who were treated with non-HyQvia treatment by time of enrollment were enrolled in Epoch 1 (ramp-up) and treated with HyQvia subcutaneously (SC) with a dose or interval ramp-up period of up to 6 weeks. HyQvia dose was planned to be equivalent to 100% ( $\pm 5\%$ ) of pre-study treatment. Dosage frequency was one treatment interval of one week, then one treatment interval of two weeks, then one treatment interval of three weeks (for subjects in whom treatment was expected to be every four weeks). The ramp-up period was followed by Epoch 2 with HyQvia SC treatment at every 3 or 4 weeks, depending on the subject's previous dosing schedule and the discretion of the investigator and subject, for up to 20 months.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | HyQvia Pre-treated |
|-----------------------|--------------------|

Reporting group description:

Subjects already treated with HYQVIA by the time of enrollment were directly enrolled in Epoch 2 and treated with HyQvia SC at every 3 or 4 weeks for up to 20 months. HyQvia dose was planned to be equivalent to 100% ( $\pm 5\%$ ) of pre-study treatment with a dosage frequency of once every three or four weeks, based on the subject's previous dosing schedule and the discretion of the investigator and subject.

| Reporting group values    | HyQvia New Starters | HyQvia Pre-treated | Total |
|---------------------------|---------------------|--------------------|-------|
| Number of subjects        | 23                  | 19                 | 42    |
| Age Categorical<br>Units: |                     |                    |       |

|                                           |            |            |    |
|-------------------------------------------|------------|------------|----|
| Age Continuous<br>Units: years            |            |            |    |
| arithmetic mean                           | 10.3       | 11.7       |    |
| standard deviation                        | $\pm 3.82$ | $\pm 4.33$ | -  |
| Gender Categorical<br>Units: Subjects     |            |            |    |
| Female                                    | 5          | 3          | 8  |
| Male                                      | 18         | 16         | 34 |
| Race<br>Units: Subjects                   |            |            |    |
| American Indian Or Alaska Native          | 0          | 0          | 0  |
| Asian                                     | 0          | 0          | 0  |
| Black Or African American                 | 0          | 0          | 0  |
| Native Hawaiian Or Other Pacific Islander | 0          | 0          | 0  |
| White                                     | 22         | 19         | 41 |
| More than one race                        | 0          | 0          | 0  |
| Unknown or Not Reported                   | 1          | 0          | 1  |
| Ethnicity<br>Units: Subjects              |            |            |    |
| Hispanic Or Latino                        | 0          | 0          | 0  |
| Not Hispanic Or Latino                    | 23         | 19         | 42 |
| Unknown or Not Reported                   | 0          | 0          | 0  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | HyQvia New Starters |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                     |
| Subjects who were treated with non-HyQvia treatment by time of enrollment were enrolled in Epoch 1 (ramp-up) and treated with HyQvia subcutaneously (SC) with a dose or interval ramp-up period of up to 6 weeks. HyQvia dose was planned to be equivalent to 100% ( $\pm 5\%$ ) of pre-study treatment. Dosage frequency was one treatment interval of one week, then one treatment interval of two weeks, then one treatment interval of three weeks (for subjects in whom treatment was expected to be every four weeks). The ramp-up period was followed by Epoch 2 with HyQvia SC treatment at every 3 or 4 weeks, depending on the subject's previous dosing schedule and the discretion of the investigator and subject, for up to 20 months. |                     |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | HyQvia Pre-treated  |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                     |
| Subjects already treated with HYQVIA by the time of enrollment were directly enrolled in Epoch 2 and treated with HyQvia SC at every 3 or 4 weeks for up to 20 months. HyQvia dose was planned to be equivalent to 100% ( $\pm 5\%$ ) of pre-study treatment with a dosage frequency of once every three or four weeks, based on the subject's previous dosing schedule and the discretion of the investigator and subject.                                                                                                                                                                                                                                                                                                                          |                     |

### Primary: Safety: Number of Subjects With Any Severe Related Treatment-emergent Adverse Events (TEAEs) per Infusion (Excluding Infections)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Safety: Number of Subjects With Any Severe Related Treatment-emergent Adverse Events (TEAEs) per Infusion (Excluding Infections) <sup>[1]</sup> |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |
| An Adverse Event (AE) was defined as any untoward medical occurrence in a subject administered an investigational product (IP) that does not necessarily have a causal relationship with the treatment. TEAEs are AEs with onset after date-time of first dose of IP, or any medical condition present prior to the start of IP but increased in severity or relationship after date-time of first dose of IP. TEAEs recorded as "possibly related" or "probably related" to HYQVIA are considered HYQVIA-related. The number of subjects with any severe related TEAEs was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. |                                                                                                                                                 |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Primary                                                                                                                                         |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                 |
| From start of study drug administration up to 20 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                 |
| Notes:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                 |
| [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                 |
| Justification: No statistical and comparison analysis were performed for this endpoint.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                 |

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 1                   | 0                  |  |  |

### Statistical analyses

No statistical analyses for this end point

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**Primary: Safety: Rate of Any Severe Related TEAEs per Infusion (Excluding Infections)**

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|                 |                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Safety: Rate of Any Severe Related TEAEs per Infusion (Excluding Infections) <sup>[2]</sup> |
|-----------------|---------------------------------------------------------------------------------------------|

End point description:

An AE was defined as any untoward medical occurrence in a subject administered an IP that does not necessarily have a causal relationship with the treatment. TEAE was defined as AEs with onset after date-time of first dose of IP, or any medical conditions present prior to the start of IP but increased in severity or relationship after date-time of first dose of IP. Severe related TEAEs rate per infusion was calculated as number of severe related TEAEs/total number of infusions administered to subjects in the analysis set. Rate of any severe related TEAEs per infusion (excluding infections) was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

Notes:

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

Justification: No statistical and comparison analysis were performed for this endpoint.

| End point values                               | HyQvia New Starters | HyQvia Pre-treated |  |  |
|------------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                             | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed                    | 23                  | 19                 |  |  |
| Units: Number of Severe Related TEAEs/Infusion |                     |                    |  |  |
| number (not applicable)                        | 0.004               | 0                  |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Primary: Safety: Number of Subjects With Any Related Serious TEAEs per Infusion (Excluding Infections)**

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|                 |                                                                                                              |
|-----------------|--------------------------------------------------------------------------------------------------------------|
| End point title | Safety: Number of Subjects With Any Related Serious TEAEs per Infusion (Excluding Infections) <sup>[3]</sup> |
|-----------------|--------------------------------------------------------------------------------------------------------------|

End point description:

TEAE was defined as AEs with onset after date-time of first dose of IP, or any medical conditions present prior to the start of IP but increased in severity or relationship after date-time of first dose of IP. A serious TEAE was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged in-patient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. Related TEAE was defined as AEs recorded in the study database as "possibly related" or "probably related" to IP. Number of subjects with any related serious TEAEs per infusion (excluding infections) were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

Notes:

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

Justification: No statistical and comparison analysis were performed for this endpoint.

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 0                   | 0                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Safety: Rate of Any Related Serious TEAEs per Infusion (Excluding Infections)

|                 |                                                                                              |
|-----------------|----------------------------------------------------------------------------------------------|
| End point title | Safety: Rate of Any Related Serious TEAEs per Infusion (Excluding Infections) <sup>[4]</sup> |
|-----------------|----------------------------------------------------------------------------------------------|

End point description:

TEAE was defined as AEs with onset after date-time of first dose of IP, or any medical conditions present prior to the start of IP but increased in severity or relationship after date-time of first dose of IP. A serious TEAE was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged in-patient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. Related TEAE was defined as AEs recorded in the study database as "possibly related" or "probably related" to IP. Rate of related serious TEAEs per infusion was calculated as number of related serious TEAEs/total number of infusions administered to subjects in the analysis set. Rate of any related serious TEAEs per Infusion (excluding infections) were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

Notes:

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

Justification: No statistical and comparison analysis were performed for this endpoint.

| End point values                                | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-------------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                              | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed                     | 23                  | 19                 |  |  |
| Units: Number of Related Serious TEAEs/Infusion |                     |                    |  |  |
| number (not applicable)                         | 0                   | 0                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Efficacy: Change From Baseline in Total Serum Trough Levels of Immunoglobulin G (IgG) at Month 12

|                 |                                                                                                   |
|-----------------|---------------------------------------------------------------------------------------------------|
| End point title | Efficacy: Change From Baseline in Total Serum Trough Levels of Immunoglobulin G (IgG) at Month 12 |
|-----------------|---------------------------------------------------------------------------------------------------|

End point description:

Change from baseline in total serum trough levels of IgG in Epoch 1 and 2 was reported. Baseline was defined as the last non-missing value before the initial dose of HYQVIA. Full analysis set included all

subjects who provided informed consent and met enrollment eligibility. Here, "number of subjects analysed" signifies subjects who were evaluable for this endpoint.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline, Month 12   |           |

| End point values                     | HyQvia New Starters   | HyQvia Pre-treated     |  |  |
|--------------------------------------|-----------------------|------------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed          | 20                    | 17                     |  |  |
| Units: Gram per liter (g/L)          |                       |                        |  |  |
| arithmetic mean (standard deviation) | 0.035 ( $\pm$ 1.6983) | -0.709 ( $\pm$ 2.6576) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Percentage of Subjects who Achieved a Treatment Interval of Three or Four Weeks in Epoch 2

|                        |                                                                                                                                                                                                                                       |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | Safety: Percentage of Subjects who Achieved a Treatment Interval of Three or Four Weeks in Epoch 2                                                                                                                                    |
| End point description: | Percentage of subjects who achieved a treatment interval of three or four weeks in Epoch 2 were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. |
| End point type         | Secondary                                                                                                                                                                                                                             |
| End point timeframe:   |                                                                                                                                                                                                                                       |
| Up to 20 months        |                                                                                                                                                                                                                                       |

| End point values                 | HyQvia New Starters | HyQvia Pre-treated |  |  |
|----------------------------------|---------------------|--------------------|--|--|
| Subject group type               | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed      | 23                  | 19                 |  |  |
| Units: Percentage of subjects    |                     |                    |  |  |
| number (not applicable)          |                     |                    |  |  |
| Every 3 weeks treatment interval | 39.1                | 15.8               |  |  |
| Every 4 weeks treatment interval | 60.9                | 84.2               |  |  |

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Safety: Percentage of Subjects who Maintained a Treatment Interval of Three or Four Weeks in Epoch 2 up to 12 Months**

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|                 |                                                                                                                      |
|-----------------|----------------------------------------------------------------------------------------------------------------------|
| End point title | Safety: Percentage of Subjects who Maintained a Treatment Interval of Three or Four Weeks in Epoch 2 up to 12 Months |
|-----------------|----------------------------------------------------------------------------------------------------------------------|

End point description:

Percentage of subjects who maintained a treatment interval of three or four weeks in Epoch 2 up to 12 months was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

Up to 12 Months

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| End point values              | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-------------------------------|---------------------|--------------------|--|--|
| Subject group type            | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed   | 23                  | 19                 |  |  |
| Units: Percentage of subjects |                     |                    |  |  |
| number (not applicable)       | 87.0                | 78.9               |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Safety: Number of Subjects With Local TEAEs (Excluding Infections)**

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|                 |                                                                    |
|-----------------|--------------------------------------------------------------------|
| End point title | Safety: Number of Subjects With Local TEAEs (Excluding Infections) |
|-----------------|--------------------------------------------------------------------|

End point description:

TEAE was defined as AEs with onset after date-time of first dose of IP, or any medical conditions present prior to the start of IP but increased in severity or relationship after date-time of first dose of IP. Number of subjects with local TEAEs (excluding infections) were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

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| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 11                  | 3                  |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

### Secondary: Safety: Rate of Local TEAEs per Infusion (Excluding Infections)

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Safety: Rate of Local TEAEs per Infusion (Excluding Infections) |
|-----------------|-----------------------------------------------------------------|

End point description:

Rate of local TEAEs per infusion was calculated as number of local adverse events/total number of infusions administered to subjects in the analysis set. Only events are included which start prior to subjects start date of non-response. Rate of local TEAEs per infusion (excluding infections) was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values                      | HyQvia New Starters | HyQvia Pre-treated |  |  |
|---------------------------------------|---------------------|--------------------|--|--|
| Subject group type                    | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed           | 23                  | 19                 |  |  |
| Units: Number of local TEAEs/Infusion |                     |                    |  |  |
| number (not applicable)               | 0.082               | 0.009              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Number of Subjects With Local Adverse Reactions (Excluding Infections)

|                 |                                                                                |
|-----------------|--------------------------------------------------------------------------------|
| End point title | Safety: Number of Subjects With Local Adverse Reactions (Excluding Infections) |
|-----------------|--------------------------------------------------------------------------------|

End point description:

Adverse reactions was defined as any TEAE that meets any of the following criteria: 1) A TEAE considered by either the investigator and/or the sponsor to be possibly or probably related to IP administration, or; 2) A TEAE that begins during infusion of IP or within 72 hours following the end of IP infusion, or; 3) A TEAE for which causality assessment is missing or indeterminate. Number of subjects with local adverse reactions (excluding infections) were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 11                  | 3                  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Rate of Local Adverse Reaction per Infusion (Excluding Infections)

|                 |                                                                            |
|-----------------|----------------------------------------------------------------------------|
| End point title | Safety: Rate of Local Adverse Reaction per Infusion (Excluding Infections) |
|-----------------|----------------------------------------------------------------------------|

End point description:

Rate of local adverse reaction per infusion was calculated as number of local adverse reaction events/total number of infusions administered to subjects in the analysis set. Rate of local adverse reactions per infusion (excluding infections) was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values                          | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                        | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed               | 23                  | 19                 |  |  |
| Units: Number of Local AR events/Infusion |                     |                    |  |  |
| number (not applicable)                   | 0.080               | 0.009              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Number of Subjects With Systemic TEAEs (Excluding Infections)

|                 |                                                                       |
|-----------------|-----------------------------------------------------------------------|
| End point title | Safety: Number of Subjects With Systemic TEAEs (Excluding Infections) |
|-----------------|-----------------------------------------------------------------------|

End point description:

TEAE was defined as AEs with onset after date-time of first dose of IP, or any medical conditions present prior to the start of IP but increased in severity or relationship after date-time of first dose of IP. Number of subjects with systemic TEAEs (excluding infections) were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 15                  | 10                 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety: Rate of Systemic TEAEs per Infusion (Excluding Infections)

|                 |                                                                    |
|-----------------|--------------------------------------------------------------------|
| End point title | Safety: Rate of Systemic TEAEs per Infusion (Excluding Infections) |
|-----------------|--------------------------------------------------------------------|

End point description:

Rate of systemic TEAEs per infusion was calculated as number of systemic adverse events/total number of infusions administered to subjects in the analysis set. Rate of systemic TEAEs per infusion was assessed based on events per infusion. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values                         | HyQvia New Starters | HyQvia Pre-treated |  |  |
|------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed              | 23                  | 19                 |  |  |
| Units: Number of systemic TEAEs/Infusion |                     |                    |  |  |
| number (not applicable)                  | 0.138               | 0.142              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety: Number of Subjects With Systemic Adverse Reactions (Excluding Infections)

|                 |                                                                                   |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | Safety: Number of Subjects With Systemic Adverse Reactions (Excluding Infections) |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

Adverse reaction was defined as any TEAE that meets any of the following criteria: 1) A TEAE considered by either the investigator and/or the sponsor to be possibly or probably related to IP administration, or; 2) A TEAE that begins during infusion of IP or within 72 hours following the end of IP infusion, or; 3) A TEAE for which causality assessment is missing or indeterminate. Number of subjects with systemic adverse reactions (excluding infections) were reported. Safety analysis set included all subjects in the

full analysis set (enrolled set) who received at least one dose of HyQvia.

|                                                         |           |
|---------------------------------------------------------|-----------|
| End point type                                          | Secondary |
| End point timeframe:                                    |           |
| From start of study drug administration up to 20 months |           |

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 3                   | 1                  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Rate of Systemic Adverse Reactions per Infusion (Excluding Infections)

|                 |                                                                                |
|-----------------|--------------------------------------------------------------------------------|
| End point title | Safety: Rate of Systemic Adverse Reactions per Infusion (Excluding Infections) |
|-----------------|--------------------------------------------------------------------------------|

End point description:

Rate of Systemic adverse reactions per infusion was calculated as number of systemic adverse reaction events/total number of infusions administered to subjects in the analysis set. Rate of systemic adverse reactions per infusion (excluding infections) was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

|                                                         |           |
|---------------------------------------------------------|-----------|
| End point type                                          | Secondary |
| End point timeframe:                                    |           |
| From start of study drug administration up to 20 months |           |

| End point values                             | HyQvia New Starters | HyQvia Pre-treated |  |  |
|----------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                           | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed                  | 23                  | 19                 |  |  |
| Units: Number of Systemic AR events/Infusion |                     |                    |  |  |
| number (not applicable)                      | 0.011               | 0.012              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Number of Subjects With Any TEAEs (Excluding Infections)

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Safety: Number of Subjects With Any TEAEs (Excluding Infections) |
|-----------------|------------------------------------------------------------------|

End point description:

TEAE was defined as AEs with onset after date-time of first dose of IP, or any medical conditions present prior to the start of IP but increased in severity or relationship after date-time of first dose of IP.

Number of subjects with any TEAEs (excluding infections) were reported. Safety analysis set included all subjects in the full analysis set (Enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 18                  | 11                 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety: Rate of TEAEs per Infusion (Excluding Infections)

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | Safety: Rate of TEAEs per Infusion (Excluding Infections) |
|-----------------|-----------------------------------------------------------|

End point description:

Rate of TEAEs per infusion was calculated as number of adverse events/total number of infusions administered to subjects in the analysis set. Rate of TEAEs per infusion (excluding infections) was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values                | HyQvia New Starters | HyQvia Pre-treated |  |  |
|---------------------------------|---------------------|--------------------|--|--|
| Subject group type              | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed     | 23                  | 19                 |  |  |
| Units: Number of TEAEs/Infusion |                     |                    |  |  |
| number (not applicable)         | 0.220               | 0.151              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety: Number of Subjects With Any Adverse Reactions (Excluding Infections)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                              |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Safety: Number of Subjects With Any Adverse Reactions (Excluding Infections) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                              |
| Adverse reaction was defined as any TEAE that meets any of the following criteria: 1) A TEAE considered by either the investigator and/or the sponsor to be possibly or probably related to IP administration, or; 2) A TEAE that begins during infusion of IP or within 72 hours following the end of IP infusion, or; 3) A TEAE for which causality assessment is missing or indeterminate. Number of subjects with any adverse reactions (excluding infections) were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. |                                                                              |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Secondary                                                                    |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                              |
| From start of study drug administration up to 20 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                              |

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 12                  | 3                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety: Rate of Any Adverse Reaction per Infusion (Excluding Infections)

|                                                                                                                                                                                                                                                                                                                                                                                   |                                                                          |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                   | Safety: Rate of Any Adverse Reaction per Infusion (Excluding Infections) |
| End point description:                                                                                                                                                                                                                                                                                                                                                            |                                                                          |
| Rate of all adverse reaction per infusion was calculated as number of adverse reaction events/total number of infusions administered to subjects in the analysis set. Rate of any adverse reactions per infusion (excluding infections) was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. |                                                                          |
| End point type                                                                                                                                                                                                                                                                                                                                                                    | Secondary                                                                |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                              |                                                                          |
| From start of study drug administration up to 20 months                                                                                                                                                                                                                                                                                                                           |                                                                          |

| End point values                       | HyQvia New Starters | HyQvia Pre-treated |  |  |
|----------------------------------------|---------------------|--------------------|--|--|
| Subject group type                     | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed            | 23                  | 19                 |  |  |
| Units: Adverse reaction event/Infusion |                     |                    |  |  |
| number (not applicable)                | 0.091               | 0.021              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Number of Subjects With Any Temporally Associated TEAEs (Excluding Infections)

|                 |                                                                                        |
|-----------------|----------------------------------------------------------------------------------------|
| End point title | Safety: Number of Subjects With Any Temporally Associated TEAEs (Excluding Infections) |
|-----------------|----------------------------------------------------------------------------------------|

End point description:

Temporally-associated TEAEs were defined as TEAEs which begin during infusion of IP or within 72 hours following the end of IP infusion. Number of subjects with any temporally associated TEAEs (excluding infections) were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 13                  | 6                  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Rate of Any Temporally Associated TEAEs per Infusion (Excluding Infections)

|                 |                                                                                     |
|-----------------|-------------------------------------------------------------------------------------|
| End point title | Safety: Rate of Any Temporally Associated TEAEs per Infusion (Excluding Infections) |
|-----------------|-------------------------------------------------------------------------------------|

End point description:

Rate of any temporally associated TEAEs per infusion was calculated as number of temporally associated adverse events/total number of infusions administered to subjects in the analysis set. Temporally-associated TEAEs were defined as TEAEs which begin during infusion of IP or within 72 hours following the end of IP infusion. Rate of any temporally associated TEAEs per infusion (excluding infections) was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values                            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|---------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed                 | 23                  | 19                 |  |  |
| Units: Temporally associated TEAEs/Infusion |                     |                    |  |  |
| number (not applicable)                     | 0.106               | 0.027              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Number of Subjects With Any Related (Causally) and/or Temporally Associated TEAEs (Excluding Infections)

|                 |                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| End point title | Safety: Number of Subjects With Any Related (Causally) and/or Temporally Associated TEAEs (Excluding Infections) |
|-----------------|------------------------------------------------------------------------------------------------------------------|

End point description:

Number of subjects with any related (causally) and/or temporally associated TEAEs (excluding infections) were reported. Temporally-associated TEAEs were defined as TEAEs which begin during infusion of IP or within 72 hours following the end of IP infusion. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 13                  | 6                  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Rate of Any Related (Causally) and/or Temporally Associated TEAEs per Infusion (Excluding Infections)

|                 |                                                                                                               |
|-----------------|---------------------------------------------------------------------------------------------------------------|
| End point title | Safety: Rate of Any Related (Causally) and/or Temporally Associated TEAEs per Infusion (Excluding Infections) |
|-----------------|---------------------------------------------------------------------------------------------------------------|

End point description:

Rate of any related (causally) and/or temporally associated TEAEs per infusion was calculated as number of related and/or temporally associated adverse events/ total number of infusions administered to subjects in the analysis set. TEAEs recorded in the study database as "possibly related" or "probably related" to HYQVIA are considered HYQVIA related adverse events. Temporally-associated TEAEs were defined as TEAEs which begin during infusion of IP or within 72 hours following the end of IP infusion. Rate of any related (causally) and/or temporally associated TEAEs per infusion (excluding infections) was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values                         | HyQvia New Starters | HyQvia Pre-treated |  |  |
|------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                       | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed              | 23                  | 19                 |  |  |
| Units: Related Temporally TEAEs/Infusion |                     |                    |  |  |
| number (not applicable)                  | 0.112               | 0.033              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety: Number of Subjects With Any Serious TEAEs (Excluding Infections)

|                 |                                                                          |
|-----------------|--------------------------------------------------------------------------|
| End point title | Safety: Number of Subjects With Any Serious TEAEs (Excluding Infections) |
|-----------------|--------------------------------------------------------------------------|

End point description:

Serious TEAE was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged in-patient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. Number of subjects with any serious TEAEs (excluding infections) were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

From start of study drug administration up to 20 months

| End point values            | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------|---------------------|--------------------|--|--|
| Subject group type          | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed | 23                  | 19                 |  |  |
| Units: Subjects             | 0                   | 3                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety: Rate of Serious TEAEs per Infusion (Excluding Infections)

|                 |                                                                   |
|-----------------|-------------------------------------------------------------------|
| End point title | Safety: Rate of Serious TEAEs per Infusion (Excluding Infections) |
|-----------------|-------------------------------------------------------------------|

End point description:

Rate of serious TEAEs per infusion was calculated as number of serious adverse events/total number of infusions administered to subjects in the analysis set. Rate of serious TEAEs per infusion (excluding infections) was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

|                                                         |           |
|---------------------------------------------------------|-----------|
| End point type                                          | Secondary |
| End point timeframe:                                    |           |
| From start of study drug administration up to 20 months |           |

| End point values                        | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------------------|---------------------|--------------------|--|--|
| Subject group type                      | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed             | 23                  | 19                 |  |  |
| Units: Number of serious TEAEs/Infusion |                     |                    |  |  |
| number (not applicable)                 | 0                   | 0.012              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Safety: Number of Subjects who Developed Positive Titer ( $\geq 160$ ) of Binding or Neutralizing Antibodies to rHuPH20

|                                                                                                                                                                                                                                                            |                                                                                                                         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                            | Safety: Number of Subjects who Developed Positive Titer ( $\geq 160$ ) of Binding or Neutralizing Antibodies to rHuPH20 |
| End point description:                                                                                                                                                                                                                                     |                                                                                                                         |
| Number of subjects who developed positive titer ( $\geq 160$ ) of binding or neutralizing antibodies to rHuPH20 were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. |                                                                                                                         |
| End point type                                                                                                                                                                                                                                             | Secondary                                                                                                               |
| End point timeframe:                                                                                                                                                                                                                                       |                                                                                                                         |
| From start of study drug administration up to 20 months                                                                                                                                                                                                    |                                                                                                                         |

| End point values                                    | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-----------------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                                  | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed                         | 23                  | 19                 |  |  |
| Units: Subjects                                     |                     |                    |  |  |
| Positive titer ( $\geq 160$ ) of binding antibodies | 0                   | 0                  |  |  |
| Neutralizing antibodies                             | 0                   | 0                  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Other Analysis: Number of Infusions per Month

|                 |                                               |
|-----------------|-----------------------------------------------|
| End point title | Other Analysis: Number of Infusions per Month |
|-----------------|-----------------------------------------------|

End point description:

Number of infusions per month was calculated as total number of infusions per duration of treatment (days) \* 30.4 days per month. Number of infusions per month was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

End point type Secondary

End point timeframe:

Up to 20 months

| End point values              | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-------------------------------|---------------------|--------------------|--|--|
| Subject group type            | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed   | 23                  | 19                 |  |  |
| Units: Infusions per month    |                     |                    |  |  |
| median (full range (min-max)) | 1.30 (1.1 to 1.7)   | 1.20 (1.0 to 1.6)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Other Analysis: Number of Infusion Sites (Needle-Sticks) per Infusion

End point title Other Analysis: Number of Infusion Sites (Needle-Sticks) per Infusion

End point description:

Number of infusion sites (needle-sticks) per infusion was calculated as total number of infusion sites / total number of infusions. Only infusions with complete data available was included. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

End point type Secondary

End point timeframe:

Up to 20 months

| End point values                               | HyQvia New Starters | HyQvia Pre-treated |  |  |
|------------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                             | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed                    | 23                  | 19                 |  |  |
| Units: Infusion sites (needle sticks)/Infusion |                     |                    |  |  |
| arithmetic mean (standard deviation)           | 1.65 (± 0.442)      | 1.25 (± 0.403)     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Other Analysis: Duration of Infusion

|                                                                                                                                                                                                                                                                              |                                      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| End point title                                                                                                                                                                                                                                                              | Other Analysis: Duration of Infusion |
| End point description:<br>The duration of infusion was defined as the difference between the end time and the start time of the HyQvia infusion. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. |                                      |
| End point type                                                                                                                                                                                                                                                               | Secondary                            |
| End point timeframe:<br>From start of study drug administration up to 20 months                                                                                                                                                                                              |                                      |

| End point values              | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-------------------------------|---------------------|--------------------|--|--|
| Subject group type            | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed   | 23                  | 19                 |  |  |
| Units: Minutes                |                     |                    |  |  |
| median (full range (min-max)) | 75.0 (10 to 215)    | 101.0 (15 to 257)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Other Analysis: Maximum Infusion Rate per Site

|                                                                                                                                                                                                    |                                                |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|
| End point title                                                                                                                                                                                    | Other Analysis: Maximum Infusion Rate per Site |
| End point description:<br>Maximum infusion rate per site was reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. |                                                |
| End point type                                                                                                                                                                                     | Secondary                                      |
| End point timeframe:<br>Up to 20 months                                                                                                                                                            |                                                |

| End point values                                | HyQvia New Starters | HyQvia Pre-treated |  |  |
|-------------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                              | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed                     | 23                  | 19                 |  |  |
| Units: Milliliter per hour per site (mL/h/site) |                     |                    |  |  |
| arithmetic mean (standard deviation)            | 181.54 (± 77.772)   | 171.73 (± 90.203)  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Other Analysis: Infusion Volume per Site

|                 |                                          |
|-----------------|------------------------------------------|
| End point title | Other Analysis: Infusion Volume per Site |
|-----------------|------------------------------------------|

End point description:

Infusion volume per site was calculated as actual IgG volume (milliliter [mL]) per total number of infusion sites (hour) used. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

Up to 20 months

| End point values                     | HyQvia New Starters    | HyQvia Pre-treated     |  |  |
|--------------------------------------|------------------------|------------------------|--|--|
| Subject group type                   | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed          | 23                     | 19                     |  |  |
| Units: milliliter per hour           |                        |                        |  |  |
| arithmetic mean (standard deviation) | 112.39 ( $\pm$ 71.427) | 178.23 ( $\pm$ 98.523) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Other Analysis: Number of Infusions That Were Interrupted or Stopped due to an AE

|                 |                                                                                   |
|-----------------|-----------------------------------------------------------------------------------|
| End point title | Other Analysis: Number of Infusions That Were Interrupted or Stopped due to an AE |
|-----------------|-----------------------------------------------------------------------------------|

End point description:

Number of infusions that were interrupted or stopped due to an AE were reported. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

Up to 20 months

| End point values                | HyQvia New Starters | HyQvia Pre-treated |  |  |
|---------------------------------|---------------------|--------------------|--|--|
| Subject group type              | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed     | 23                  | 19                 |  |  |
| Units: Infusions                |                     |                    |  |  |
| number (not applicable)         |                     |                    |  |  |
| Number of infusions interrupted | 4                   | 0                  |  |  |
| Number of infusions Stopped     | 1                   | 0                  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Other Analysis: Number of Weeks to Reach Final 3 or 4-week Dose Interval in Epoch 1

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Other Analysis: Number of Weeks to Reach Final 3 or 4-week Dose Interval in Epoch 1 <sup>[5]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Final dose interval was defined as three or four weeks infusion interval in Epoch 1 of treatment period was reported. Safety analysis set included all subjects in the full analysis set (enrolled Set) who received at least one dose of HyQvia. Here, "number analysed" signifies subjects who are evaluable for this endpoint.

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

End point timeframe:

Up to 20 months

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As pre-specified in protocol, Data collection and analysis was not planned for HyQvia pre-treated.

|                               |                     |  |  |  |
|-------------------------------|---------------------|--|--|--|
| <b>End point values</b>       | HyQvia New Starters |  |  |  |
| Subject group type            | Reporting group     |  |  |  |
| Number of subjects analysed   | 22                  |  |  |  |
| Units: Weeks                  |                     |  |  |  |
| median (full range (min-max)) | 6.10 (3.0 to 7.0)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Health Related Quality of Life (HR QoL): Change from Baseline in Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9)

|                 |                                                                                                                                 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Health Related Quality of Life (HR QoL): Change from Baseline in Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9) |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

TSQM-9 is a 9-item, validated, self-administered instrument to assess subjects satisfaction with medication. It consists of 3 sub-scales: effectiveness, convenience and global satisfaction. The scores were computed by adding items for each domain, i.e. 1 to 3 for effectiveness, 4 - 6 for convenience and 7 to 9 for global satisfaction. The lowest possible score (1 for each item and 3 for all 3 sub-scales) was subtracted from the composite score and divided by the greatest possible score range. The greatest range was  $(7-1)*3$  items = 18 for the effectiveness and convenience, and  $(5-1)*3$  items = 12 for global satisfaction. The item scores of each of the 3 domains are summed and transformed to create a score of 0 (extremely dissatisfied) to 100 (extremely satisfied). Higher score=greater satisfaction in that domain. A negative change from baseline indicates less satisfaction in that domain. Safety analysis set. Here, "number of subjects analysed"= subjects evaluable for this endpoint.

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

End point timeframe:

Baseline up to 20 months

| End point values                      | HyQvia New Starters | HyQvia Pre-treated |  |  |
|---------------------------------------|---------------------|--------------------|--|--|
| Subject group type                    | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed           | 3                   | 6                  |  |  |
| Units: Score on a scale               |                     |                    |  |  |
| arithmetic mean (standard deviation)  |                     |                    |  |  |
| Effectiveness: Change at 20 months    | 12.96 (± 32.552)    | -0.92 (± 10.783)   |  |  |
| Convenience: Change at 20 months      | 14.81 (± 27.398)    | 4.63 (± 15.873)    |  |  |
| Global satisfaction: Change 20 months | 11.90 (± 10.911)    | -2.38 (± 19.518)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: HRQoL: Change from Baseline in Pediatric Quality of Life Questionnaire (PedsQL)

|                 |                                                                                 |
|-----------------|---------------------------------------------------------------------------------|
| End point title | HRQoL: Change from Baseline in Pediatric Quality of Life Questionnaire (PedsQL) |
|-----------------|---------------------------------------------------------------------------------|

End point description:

PedsQL Generic Core Scale (GCS) used for QOL assessment. It encompasses 4 dimensions (physical functioning [PF], emotional functioning [EF], social functioning [SF], school functioning [ScF]). Age groups: Toddler (2-4 years), Young child (5-7 years), Child (8-12 years) and Teens (13-<18 years). Depending on the subjects age, the questionnaire may be completed by either the subject or the parent/caregiver. For Toddler, PedsQL GCS as 21 items, using 5-point Likert scale (0 to 4); for all other, PedsQL as 23 items, with 3-point Likert scale (0, 2, 4) for young child, and 5-point Likert scale for child and teens. All scores were transformed on a scale from 0-100 where 0=100, 1=75, 2=50, 3=25 and 4=0. Higher scores= better quality of life. A negative change from baseline=worse quality of life. Safety analysis set. Here, "number of subjects analysed"= subjects evaluable for this endpoint and "n=number analysed" evaluable at specific timepoint. Here, '99999' = mean and SD was not estimated.

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

End point timeframe:

Baseline up to 20 months

| End point values                                  | HyQvia New Starters | HyQvia Pre-treated |  |  |
|---------------------------------------------------|---------------------|--------------------|--|--|
| Subject group type                                | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed                       | 5                   | 8                  |  |  |
| Units: Score on a scale                           |                     |                    |  |  |
| arithmetic mean (standard deviation)              |                     |                    |  |  |
| PF in Toddler: Change up to 20 months (n=0,1)     | 99999 (± 99999)     | -3.12 (± 99999)    |  |  |
| PF in Young child: Change up to 20 months (n=0,1) | 99999 (± 99999)     | -31.25 (± 99999)   |  |  |
| PF in Child: Change up to 20 months (n=2,1)       | 7.81 (± 6.626)      | -71.88 (± 99999)   |  |  |

|                                                    |                   |                   |  |  |
|----------------------------------------------------|-------------------|-------------------|--|--|
| PF in Teens: Change up to 20 months (n=3,5)        | -12.65 (± 12.726) | 13.75 (± 24.664)  |  |  |
| EF in Toddler: Change up to 20 months (n=0,1)      | 99999 (± 99999)   | 0.00 (± 99999)    |  |  |
| EF in Young child: Change up to 20 months (n=0,1)  | 99999 (± 99999)   | -25.00 (± 99999)  |  |  |
| EF in Child: Change up to 20 months (n=2,1)        | 5.00 (± 14.142)   | -20.00 (± 99999)  |  |  |
| EF in Teens: Change up to 20 months (n=3,5)        | -13.33 (± 7.638)  | 1.25 (± 14.307)   |  |  |
| SF in Toddler: Change up to 20 months (n=0,1)      | 99999 (± 99999)   | 0.00 (± 99999)    |  |  |
| SF in Young child: Change up to 20 months (n=0,1)  | 99999 (± 99999)   | -35.00 (± 99999)  |  |  |
| SF in Child: Change up to 20 months (n=2,1)        | -20.00 (± 0.000)  | -40.00 (± 99999)  |  |  |
| SF in Teens: Change up to 20 months (n=3,5)        | 1.67 (± 7.638)    | 8.00 (± 11.511)   |  |  |
| ScF in Toddler: Change up to 20 months (n=0,1)     | 99999 (± 99999)   | 25.00 (± 99999)   |  |  |
| ScF in Young child: Change up to 20 months (n=0,1) | 99999 (± 99999)   | -45.00 (± 99999)  |  |  |
| ScF in Child: Change up to 20 months (n=2,1)       | -12.50 (± 10.607) | -65.00 (± 99999)  |  |  |
| ScF in Teens: Change up to 20 months (n=3,5)       | 1.67 (± 7.638)    | -17.00 (± 24.135) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: HRQoL: Change from Baseline in EuroQoL (Quality of Life)-5 Dimensions (EQ-5D)

|                 |                                                                               |
|-----------------|-------------------------------------------------------------------------------|
| End point title | HRQoL: Change from Baseline in EuroQoL (Quality of Life)-5 Dimensions (EQ-5D) |
|-----------------|-------------------------------------------------------------------------------|

End point description:

EQ-5D considered five attributes of QOL evaluation, that is, mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. Each dimension had five possible levels: 1 (no problems); 2 (slight problems); 3 (moderate problems); 4 (severe problems), and; 5 (extreme problems). The subjects rating of their current HRQoL state was recorded using a standard vertical 20-cm visual analog scale (EQ-VAS), which ranged from 0 to 100, where 0 indicated worst imaginable health state and 100 was best imaginable health state. Baseline was defined as the last non-missing value before the initial dose of HYQVIA. A negative change from baseline indicates worse health state. Safety analysis set. Here, "number of subjects analysed"= subjects evaluable for this endpoint.

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

End point timeframe:

Baseline up to 20 months

| End point values                     | HyQvia New Starters   | HyQvia Pre-treated    |  |  |
|--------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed          | 5                     | 7                     |  |  |
| Units: Score on a scale              |                       |                       |  |  |
| arithmetic mean (standard deviation) | -8.60 ( $\pm$ 11.149) | -4.43 ( $\pm$ 15.447) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy: Change From Baseline in Serum Trough Levels of IgG Subclasses at Month 12

|                 |                                                                                     |
|-----------------|-------------------------------------------------------------------------------------|
| End point title | Efficacy: Change From Baseline in Serum Trough Levels of IgG Subclasses at Month 12 |
|-----------------|-------------------------------------------------------------------------------------|

End point description:

Change from baseline in serum trough levels of IgG subclasses 1, 2, 3, and 4 in Epoch 1 and 2 was reported. Baseline was defined as the last non-missing value before the initial dose of HYQVIA. All subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. Here, "number of subjects analysed" signifies subjects who were evaluable for endpoint.

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

End point timeframe:

Baseline, Month 12

| End point values                     | HyQvia New Starters    | HyQvia Pre-treated     |  |  |
|--------------------------------------|------------------------|------------------------|--|--|
| Subject group type                   | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed          | 16                     | 15                     |  |  |
| Units: g/L                           |                        |                        |  |  |
| arithmetic mean (standard deviation) |                        |                        |  |  |
| IgG Subclass 1 : Changed at Month 12 | -0.813 ( $\pm$ 1.1087) | -0.467 ( $\pm$ 1.5976) |  |  |
| IgG Subclass 2 : Changed at Month 12 | 0.000 ( $\pm$ 0.8944)  | -0.667 ( $\pm$ 1.3452) |  |  |
| IgG Subclass 3 : Changed at Month 12 | 0.000 ( $\pm$ 0.3651)  | 0.133 ( $\pm$ 0.3519)  |  |  |
| IgG Subclass 4 : Changed at Month 12 | 0.094 ( $\pm$ 0.0854)  | -0.027 ( $\pm$ 0.0799) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy: Change From Baseline in Trough Levels of Specific Antibodies to Clostridium Tetani Toxoid IgG at Month 12

|                 |                                                                                                                                    |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Efficacy: Change From Baseline in Trough Levels of Specific Antibodies to Clostridium Tetani Toxoid IgG at Month 12 <sup>[6]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------|

**End point description:**

Change from baseline in trough levels of specific antibodies in clostridium tetani toxoid IgG at Month 12 was reported. Baseline was defined as the last non-missing value before the initial dose of HYQVIA. Here, IU/ml was defined as "International units per milliliter". All subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. Here, "number of subjects analysed" signifies subjects who were evaluable for endpoint.

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

**End point timeframe:**

Baseline, Month 12

**Notes:**

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Specific antibody data were not scheduled to be collected at Epoch 2 Month 0, so for most subjects baseline could not be defined and change from baseline was not reported in HYQVIA Pre-treated arm.

| End point values                     | HyQvia New Starters    |  |  |  |
|--------------------------------------|------------------------|--|--|--|
| Subject group type                   | Reporting group        |  |  |  |
| Number of subjects analysed          | 21                     |  |  |  |
| Units: IU/ml                         |                        |  |  |  |
| arithmetic mean (standard deviation) | -0.218 ( $\pm$ 0.9345) |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Efficacy: Change From Baseline in Trough Levels of Specific Antibodies to Hepatitis B Virus (HBV) at Month 12**

|                 |                                                                                                                              |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|
| End point title | Efficacy: Change From Baseline in Trough Levels of Specific Antibodies to Hepatitis B Virus (HBV) at Month 12 <sup>[7]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|

**End point description:**

Change from baseline in trough levels of specific antibodies in HBV at Month 12 was reported. Baseline was defined as the last non-missing value before the initial dose of HYQVIA. All subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. Here, "number of subjects analysed" signifies subjects who were evaluable for endpoint.

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

**End point timeframe:**

Baseline, Month 12

**Notes:**

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Specific antibody data were not scheduled to be collected at Epoch 2 Month 0, so for most subjects baseline could not be defined and change from baseline was not reported in HYQVIA Pre-treated arm.

| End point values                            | HyQvia New Starters       |  |  |  |
|---------------------------------------------|---------------------------|--|--|--|
| Subject group type                          | Reporting group           |  |  |  |
| Number of subjects analysed                 | 16                        |  |  |  |
| Units: International units per liter (IU/L) |                           |  |  |  |
| arithmetic mean (standard deviation)        | 167.875 ( $\pm$ 147.4887) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Efficacy: Change From Baseline in Trough Levels of Specific Antibodies to Haemophilus influenzae B IgG at Month 12

|                 |                                                                                                                                   |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|
| End point title | Efficacy: Change From Baseline in Trough Levels of Specific Antibodies to Haemophilus influenzae B IgG at Month 12 <sup>[8]</sup> |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|

End point description:

Change from baseline in trough levels of specific antibodies in Haemophilus influenzae B IgG at Month 12 was reported. Baseline was defined as the last non-missing value before the initial dose of HYQVIA. All subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia. Here, "number of subjects analysed" signifies subjects who were evaluable for endpoint.

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

End point timeframe:

Baseline, Month 12

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Specific antibody data were not scheduled to be collected at Epoch 2 Month 0, so for most subjects baseline could not be defined and change from baseline was not reported in HYQVIA Pre-treated arm.

|                                      |                        |  |  |  |
|--------------------------------------|------------------------|--|--|--|
| End point values                     | HyQvia New Starters    |  |  |  |
| Subject group type                   | Reporting group        |  |  |  |
| Number of subjects analysed          | 20                     |  |  |  |
| Units: Milligram per liter (mg/L)    |                        |  |  |  |
| arithmetic mean (standard deviation) | -0.017 ( $\pm$ 0.9503) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Other Analysis: Number of Infusion Sites (Needle-Sticks) per Month

|                 |                                                                    |
|-----------------|--------------------------------------------------------------------|
| End point title | Other Analysis: Number of Infusion Sites (Needle-Sticks) per Month |
|-----------------|--------------------------------------------------------------------|

End point description:

Number of infusion sites per month was calculated as total number of infusion sites / duration of treatment (days) \* 30.4 days. Only infusions with complete data available was included. Safety analysis set included all subjects in the full analysis set (enrolled set) who received at least one dose of HyQvia.

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

End point timeframe:

Up to 20 months

| <b>End point values</b>                     | HyQvia New Starters | HyQvia Pre-treated  |  |  |
|---------------------------------------------|---------------------|---------------------|--|--|
| Subject group type                          | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed                 | 23                  | 19                  |  |  |
| Units: Infusion sites (needle sticks)/Month |                     |                     |  |  |
| arithmetic mean (standard deviation)        | 1.96 ( $\pm$ 0.780) | 1.33 ( $\pm$ 0.634) |  |  |

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration up to end of the study (up to 43 months)

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | HyQvia New Starters |
|-----------------------|---------------------|

Reporting group description:

Subjects who were treated with non-HyQvia treatment by time of enrollment were enrolled in Epoch 1 (ramp-up) and treated with HyQvia SC with a dose or interval ramp-up period of up to 6 weeks. HyQvia dose was planned to be equivalent to 100% ( $\pm 5\%$ ) of pre-study treatment. Dosage Frequency was one treatment interval of one week, then one treatment interval of two weeks, then one treatment interval of three weeks (for subjects in whom treatment was expected to be every four weeks). The ramp-up period was followed by Epoch 2 (no ramp-up) with HyQvia SC treatment at every 3 or 4 weeks, depending on the subjects previous dosing schedule and the discretion of the investigator and subject, for up to 20 months.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | HyQvia Pre-treated |
|-----------------------|--------------------|

Reporting group description:

Subjects already treated with HYQVIA by the time of enrollment were directly enrolled in Epoch 2 and treated with HyQvia SC at every 3 or 4 weeks for up to 20 months. HyQvia dose was planned to be equivalent to 100% ( $\pm 5\%$ ) of pre-study treatment with a dosage frequency of once every three or four weeks, based on the subjects previous dosing schedule and the discretion of the investigator and subject.

| Serious adverse events                               | HyQvia New Starters | HyQvia Pre-treated |  |
|------------------------------------------------------|---------------------|--------------------|--|
| Total subjects affected by serious adverse events    |                     |                    |  |
| subjects affected / exposed                          | 2 / 23 (8.70%)      | 5 / 19 (26.32%)    |  |
| number of deaths (all causes)                        | 0                   | 0                  |  |
| number of deaths resulting from adverse events       | 0                   | 0                  |  |
| General disorders and administration site conditions |                     |                    |  |
| Pyrexia                                              |                     |                    |  |
| alternative assessment type: Systematic              |                     |                    |  |
| subjects affected / exposed                          | 0 / 23 (0.00%)      | 1 / 19 (5.26%)     |  |
| occurrences causally related to treatment / all      | 0 / 0               | 0 / 1              |  |
| deaths causally related to treatment / all           | 0 / 0               | 0 / 0              |  |
| Eye disorders                                        |                     |                    |  |
| Idiopathic orbital inflammation                      |                     |                    |  |
| alternative assessment type: Systematic              |                     |                    |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 23 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| <b>Gastrointestinal disorders</b>               |                |                |  |
| Dental caries                                   |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 23 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Inflammatory bowel disease                      |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 23 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| <b>Infections and infestations</b>              |                |                |  |
| Pharyngitis                                     |                |                |  |
| subjects affected / exposed                     | 1 / 23 (4.35%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pilonidal cyst                                  |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 23 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia                                       |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 1 / 23 (4.35%) | 0 / 19 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute sinusitis                                 |                |                |  |
| subjects affected / exposed                     | 0 / 23 (0.00%) | 1 / 19 (5.26%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| 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>                                   | HyQvia New Starters | HyQvia Pre-treated |  |
|---------------------------------------------------------------------|---------------------|--------------------|--|
| Total subjects affected by non-serious adverse events               |                     |                    |  |
| subjects affected / exposed                                         | 22 / 23 (95.65%)    | 14 / 19 (73.68%)   |  |
| Investigations                                                      |                     |                    |  |
| Blood immunoglobulin G decreased                                    |                     |                    |  |
| subjects affected / exposed                                         | 0 / 23 (0.00%)      | 1 / 19 (5.26%)     |  |
| occurrences (all)                                                   | 0                   | 1                  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                     |                    |  |
| Haemangioma                                                         |                     |                    |  |
| subjects affected / exposed                                         | 0 / 23 (0.00%)      | 1 / 19 (5.26%)     |  |
| occurrences (all)                                                   | 0                   | 1                  |  |
| Injury, poisoning and procedural complications                      |                     |                    |  |
| Contusion                                                           |                     |                    |  |
| subjects affected / exposed                                         | 1 / 23 (4.35%)      | 1 / 19 (5.26%)     |  |
| occurrences (all)                                                   | 1                   | 1                  |  |
| Radius fracture                                                     |                     |                    |  |
| subjects affected / exposed                                         | 0 / 23 (0.00%)      | 1 / 19 (5.26%)     |  |
| occurrences (all)                                                   | 0                   | 1                  |  |
| Nervous system disorders                                            |                     |                    |  |
| Headache                                                            |                     |                    |  |
| subjects affected / exposed                                         | 2 / 23 (8.70%)      | 0 / 19 (0.00%)     |  |
| occurrences (all)                                                   | 3                   | 0                  |  |
| Blood and lymphatic system disorders                                |                     |                    |  |
| Neutropenia                                                         |                     |                    |  |
| alternative assessment type: Systematic                             |                     |                    |  |
| subjects affected / exposed                                         | 0 / 23 (0.00%)      | 1 / 19 (5.26%)     |  |
| occurrences (all)                                                   | 0                   | 1                  |  |
| General disorders and administration site conditions                |                     |                    |  |
| Application site pruritus                                           |                     |                    |  |
| subjects affected / exposed                                         | 0 / 23 (0.00%)      | 1 / 19 (5.26%)     |  |
| occurrences (all)                                                   | 0                   | 1                  |  |
| Fatigue                                                             |                     |                    |  |
| subjects affected / exposed                                         | 3 / 23 (13.04%)     | 1 / 19 (5.26%)     |  |
| occurrences (all)                                                   | 3                   | 2                  |  |

|                                                                                                                                             |                       |                      |  |
|---------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------------------|--|
| Infusion site erythema<br>subjects affected / exposed<br>occurrences (all)                                                                  | 2 / 23 (8.70%)<br>2   | 0 / 19 (0.00%)<br>0  |  |
| Infusion site pain<br>subjects affected / exposed<br>occurrences (all)                                                                      | 6 / 23 (26.09%)<br>11 | 1 / 19 (5.26%)<br>1  |  |
| Infusion site pruritus<br>subjects affected / exposed<br>occurrences (all)                                                                  | 4 / 23 (17.39%)<br>6  | 0 / 19 (0.00%)<br>0  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                                                                                 | 3 / 23 (13.04%)<br>5  | 3 / 19 (15.79%)<br>7 |  |
| Eye disorders<br>Conjunctival haemorrhage<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all) | 0 / 23 (0.00%)<br>0   | 1 / 19 (5.26%)<br>1  |  |
| Eye pain<br>subjects affected / exposed<br>occurrences (all)                                                                                | 1 / 23 (4.35%)<br>1   | 1 / 19 (5.26%)<br>1  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                                 | 1 / 23 (4.35%)<br>1   | 1 / 19 (5.26%)<br>5  |  |
| Inflammatory bowel disease<br>subjects affected / exposed<br>occurrences (all)                                                              | 0 / 23 (0.00%)<br>0   | 1 / 19 (5.26%)<br>1  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                                                                | 2 / 23 (8.70%)<br>4   | 1 / 19 (5.26%)<br>2  |  |
| Reproductive system and breast disorders<br>Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 23 (0.00%)<br>0   | 1 / 19 (5.26%)<br>1  |  |
| Respiratory, thoracic and mediastinal disorders                                                                                             |                       |                      |  |

|                                            |                 |                 |  |
|--------------------------------------------|-----------------|-----------------|--|
| Bronchiectasis                             |                 |                 |  |
| subjects affected / exposed                | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  |  |
| occurrences (all)                          | 0               | 1               |  |
| Cough                                      |                 |                 |  |
| subjects affected / exposed                | 8 / 23 (34.78%) | 6 / 19 (31.58%) |  |
| occurrences (all)                          | 13              | 12              |  |
| Epistaxis                                  |                 |                 |  |
| subjects affected / exposed                | 2 / 23 (8.70%)  | 2 / 19 (10.53%) |  |
| occurrences (all)                          | 2               | 6               |  |
| Oropharyngeal pain                         |                 |                 |  |
| subjects affected / exposed                | 2 / 23 (8.70%)  | 2 / 19 (10.53%) |  |
| occurrences (all)                          | 4               | 2               |  |
| Rhinorrhoea                                |                 |                 |  |
| alternative assessment type:<br>Systematic |                 |                 |  |
| subjects affected / exposed                | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  |  |
| occurrences (all)                          | 0               | 1               |  |
| Skin and subcutaneous tissue disorders     |                 |                 |  |
| Pruritus                                   |                 |                 |  |
| subjects affected / exposed                | 2 / 23 (8.70%)  | 0 / 19 (0.00%)  |  |
| occurrences (all)                          | 2               | 0               |  |
| Solar urticaria                            |                 |                 |  |
| subjects affected / exposed                | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  |  |
| occurrences (all)                          | 0               | 1               |  |
| Infections and infestations                |                 |                 |  |
| Acute sinusitis                            |                 |                 |  |
| subjects affected / exposed                | 1 / 23 (4.35%)  | 1 / 19 (5.26%)  |  |
| occurrences (all)                          | 1               | 1               |  |
| Bacterial infection                        |                 |                 |  |
| subjects affected / exposed                | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  |  |
| occurrences (all)                          | 0               | 1               |  |
| Bronchitis                                 |                 |                 |  |
| subjects affected / exposed                | 2 / 23 (8.70%)  | 0 / 19 (0.00%)  |  |
| occurrences (all)                          | 2               | 0               |  |
| Gastroenteritis                            |                 |                 |  |
| subjects affected / exposed                | 5 / 23 (21.74%) | 0 / 19 (0.00%)  |  |
| occurrences (all)                          | 7               | 0               |  |

|                                   |                 |                 |
|-----------------------------------|-----------------|-----------------|
| Gastroenteritis viral             |                 |                 |
| subjects affected / exposed       | 2 / 23 (8.70%)  | 0 / 19 (0.00%)  |
| occurrences (all)                 | 2               | 0               |
| Impetigo                          |                 |                 |
| subjects affected / exposed       | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  |
| occurrences (all)                 | 0               | 1               |
| Lower respiratory tract infection |                 |                 |
| subjects affected / exposed       | 2 / 23 (8.70%)  | 0 / 19 (0.00%)  |
| occurrences (all)                 | 3               | 0               |
| Nasopharyngitis                   |                 |                 |
| subjects affected / exposed       | 5 / 23 (21.74%) | 1 / 19 (5.26%)  |
| occurrences (all)                 | 6               | 1               |
| Otitis media                      |                 |                 |
| subjects affected / exposed       | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  |
| occurrences (all)                 | 0               | 1               |
| Pharyngotonsillitis               |                 |                 |
| subjects affected / exposed       | 0 / 23 (0.00%)  | 1 / 19 (5.26%)  |
| occurrences (all)                 | 0               | 1               |
| Pneumonia                         |                 |                 |
| subjects affected / exposed       | 0 / 23 (0.00%)  | 2 / 19 (10.53%) |
| occurrences (all)                 | 0               | 2               |
| Respiratory tract infection       |                 |                 |
| subjects affected / exposed       | 0 / 23 (0.00%)  | 2 / 19 (10.53%) |
| occurrences (all)                 | 0               | 2               |
| Rhinitis                          |                 |                 |
| subjects affected / exposed       | 3 / 23 (13.04%) | 6 / 19 (31.58%) |
| occurrences (all)                 | 4               | 12              |
| Sinusitis                         |                 |                 |
| subjects affected / exposed       | 1 / 23 (4.35%)  | 1 / 19 (5.26%)  |
| occurrences (all)                 | 1               | 1               |
| Upper respiratory tract infection |                 |                 |
| subjects affected / exposed       | 0 / 23 (0.00%)  | 3 / 19 (15.79%) |
| occurrences (all)                 | 0               | 3               |
| Viral infection                   |                 |                 |
| subjects affected / exposed       | 3 / 23 (13.04%) | 0 / 19 (0.00%)  |
| occurrences (all)                 | 4               | 0               |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 07 October 2016  | Amendment 1: <ul style="list-style-type: none"><li>- To update the study termination/completion criteria for subjects entering Epoch 3.</li><li>- To change the reference information for KIOVIG from IB to SmPC.</li><li>- To match the dosing frequency suggestions of the SmPC for Cuvitru.</li><li>- To update the study inclusion criteria.</li><li>- To provide information on Cuvitru instead of SUBCUVIA.</li><li>- To specify timelines for screening, to provide an option to treat the subject in the time period between signing the informed consent and first IP infusion, and to limit the number of re-screenings.</li><li>- To define the timepoint for blood drawing for all trough level measurements.</li><li>- To remove 'HRQoL assessments' from the Epoch 3 data under Table 6.</li><li>- To define the timepoint for blood drawing for all trough level measurements.</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                    |
| 04 December 2019 | Amendment 2: <ul style="list-style-type: none"><li>- To revise duration of study periods and subject participation till 2023 scenario in case 'last subject in' went until Epoch 2 Year 3 and then 1 year in Epoch 3.</li><li>- To clarify that safety follow-up and the antibody testing were to continue for one year, not less, for all subjects who switched to Epoch 3.</li><li>- To add 'planned interim analysis' for the study into the study protocol.</li><li>- To update the HyQvia indication for the European region.</li><li>- To add reference for the Cuvitru IB for countries where sites were open but Cuvitru was not registered.</li><li>- To provide update on the study status during the protocol amendment 2.</li><li>- To update to the latest version of GCP E6 guideline (Nov 2016) and to add 'Declaration of Helsinki' in the 'compliance statement' section.</li><li>- To add a description to allow shorter infusion intervals (2 weeks, instead of 3 or 4 weeks) if preferable due to tolerability, at the discretion of the investigator.</li><li>- To clarify in Table 8 that for some subjects Month 0 of Epoch 2 was to be considered as baseline for those subjects who did not have to participate in Epoch 2; therefore specific antibody tests also had to be performed.</li></ul> |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported