



## Clinical trial results:

A phase IV, single-blind, randomised, controlled, multi-country study to evaluate the immunogenicity and safety of GSK's Infanrix hexa (DTPa-HBV-IPV/Hib) versus MCM Vaccine BV's Vaxelis (DTaP5 HBV IPV Hib), when administered intramuscularly according to a 2 , 4 and 12 month schedule in healthy infants and toddlers.

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2019-002988-10   |
| Trial protocol           | DE IT            |
| Global end of trial date | 10 November 2022 |

### Results information

|                                |             |
|--------------------------------|-------------|
| Result version number          | v1          |
| This version publication date  | 24 May 2023 |
| First version publication date | 24 May 2023 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 212645 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04535037 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                                    |
|------------------------------|----------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | GlaxoSmithKline Biologicals SA                                                                     |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330                                                   |
| Public contact               | GSK Response Center, GlaxoSmithKline Biologicals SA, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | GSK Response Center, GlaxoSmithKline Biologicals SA, 044 2089-904466, GSKClinicalSupportHD@gsk.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                       | 12 January 2023  |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 10 November 2022 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that the Hib response in DTPa-HBV-IPV/Hib investigational group is non-inferior to DTaP5 HBV IPV Hib comparator group, 1-month post-booster vaccination in terms of geometric mean concentrations (GMCs) and percentage of subjects with anti-polyribosylribitol phosphate (PRP) antibody concentrations equal to or above ( $\geq$ ) 5 microgram per milliliter ( $\mu\text{g/mL}$ ).

To demonstrate that the Hib response in DTPa-HBV-IPV/Hib investigational group is superior to DTaP5 HBV IPV Hib comparator group, 1 month post-booster vaccination in terms of GMCs and percentage of subjects with anti-PRP antibody concentrations  $\geq 5 \mu\text{g/mL}$ . A hierarchical procedure is used to these primary objectives.

Protection of trial subjects:

Subjects must be observed closely for at least 30 minutes after the administration of the vaccines. Appropriate medical treatment must be readily available during the observation period in case of anaphylaxis and/or syncope. Vaccines/products will be administered by qualified and trained personnel. Vaccines/products will be administered only to eligible participants who have no contraindications to any components of the vaccines/products. Participants will be followed-up for 31 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 17 February 2021 |
| 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 | Germany: 150 |
| Country: Number of subjects enrolled | Italy: 20    |
| Country: Number of subjects enrolled | Spain: 330   |
| Worldwide total number of subjects   | 500          |
| EEA total number of subjects         | 500          |

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) | 500 |
| Children (2-11 years)                    | 0   |
| Adolescents (12-17 years)                | 0   |
| Adults (18-64 years)                     | 0   |
| From 65 to 84 years                      | 0   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 500 participants were enrolled in the study.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Single blind <sup>[1]</sup>    |
| Roles blinded                | Subject, Data analyst          |

### Arms

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

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Infanrix Hexa |
|------------------|---------------|

Arm description:

All subjects in this group received 3 doses (2 primary doses and 1 booster dose) of DTPa-HBV-IPV/Hib vaccine co-administered with 3 doses of pneumococcal 13 valent conjugate vaccine at 2, 4, and 12 months of age.

|                                        |                                          |
|----------------------------------------|------------------------------------------|
| Arm type                               | Experimental                             |
| Investigational medicinal product name | Prevenar 13                              |
| Investigational medicinal product code |                                          |
| Other name                             | Pneumococcal 13 valent conjugate vaccine |
| Pharmaceutical forms                   | Suspension for injection                 |
| Routes of administration               | Intramuscular use                        |

Dosage and administration details:

3 doses (1 each at 2, 4 and 12 months of age) of pneumococcal 13 valent conjugate vaccine administered by intramuscular injection into the left thigh.

|                                        |                                                    |
|----------------------------------------|----------------------------------------------------|
| Investigational medicinal product name | Infanrix hexa                                      |
| Investigational medicinal product code |                                                    |
| Other name                             | DTPa-HBV-IPV/Hib                                   |
| Pharmaceutical forms                   | Powder and suspension for suspension for injection |
| Routes of administration               | Intramuscular use                                  |

Dosage and administration details:

3 doses (1 each at 2, 4 and 12 months of age) of Infanrix hexa vaccine administered by intramuscular injection into the right thigh.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Vaxelis |
|------------------|---------|

Arm description:

All subjects in this group received 3 doses (2 primary doses and 1 booster dose) of DTaP5 HBV IPV Hib vaccine co-administered with 3 doses of pneumococcal 13 valent conjugate vaccine at 2, 4, and 12 months of age.

|                                        |                          |
|----------------------------------------|--------------------------|
| Arm type                               | Active comparator        |
| Investigational medicinal product name | Vaxelis                  |
| Investigational medicinal product code |                          |
| Other name                             | DTaP5 HBV IPV Hib        |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Intramuscular use        |

Dosage and administration details:

3 doses (1 each at 2, 4 and 12 months of age) of DTaP5 HBV IPV Hib vaccine administered by intramuscular injection into the right thigh.

|                                        |                                          |
|----------------------------------------|------------------------------------------|
| Investigational medicinal product name | Prevenar 13                              |
| Investigational medicinal product code |                                          |
| Other name                             | Pneumococcal 13 valent conjugate vaccine |
| Pharmaceutical forms                   | Suspension for injection                 |
| Routes of administration               | Intramuscular use                        |

Dosage and administration details:

3 doses (1 each at 2, 4 and 12 months of age) of pneumococcal 13 valent conjugate vaccine administered by intramuscular injection into the left thigh.

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: As per protocol, despite the fact that this is a single-blind study, the data management and biostatistics teams will remain blinded to the study treatment until after the final database lock.

| <b>Number of subjects in period 1</b> | Infanrix Hexa | Vaxelis |
|---------------------------------------|---------------|---------|
| Started                               | 249           | 251     |
| Completed                             | 237           | 233     |
| Not completed                         | 12            | 18      |
| Consent withdrawn by subject          | 8             | 9       |
| Migrated / moved from the study area  | 1             | 4       |
| Unspecified                           | 2             | 5       |
| Protocol deviation                    | 1             | -       |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                       |               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| Reporting group title                                                                                                                                                                                                 | Infanrix Hexa |
| Reporting group description:                                                                                                                                                                                          |               |
| All subjects in this group received 3 doses (2 primary doses and 1 booster dose) of DTPa-HBV-IPV/Hib vaccine co-administered with 3 doses of pneumococcal 13 valent conjugate vaccine at 2, 4, and 12 months of age.  |               |
| Reporting group title                                                                                                                                                                                                 | Vaxelis       |
| Reporting group description:                                                                                                                                                                                          |               |
| All subjects in this group received 3 doses (2 primary doses and 1 booster dose) of DTaP5 HBV IPV Hib vaccine co-administered with 3 doses of pneumococcal 13 valent conjugate vaccine at 2, 4, and 12 months of age. |               |

| Reporting group values                             | Infanrix Hexa | Vaxelis | Total |
|----------------------------------------------------|---------------|---------|-------|
| Number of subjects                                 | 249           | 251     | 500   |
| Age categorical                                    |               |         |       |
| Units: Participants                                |               |         |       |
| In utero                                           | 0             | 0       | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0             | 0       | 0     |
| Newborns (0-27 days)                               | 0             | 0       | 0     |
| Infants and toddlers (28 days-23 months)           | 249           | 251     | 500   |
| Children (2-11 years)                              | 0             | 0       | 0     |
| Adolescents (12-17 years)                          | 0             | 0       | 0     |
| Adults (18-64 years)                               | 0             | 0       | 0     |
| From 65-84 years                                   | 0             | 0       | 0     |
| 85 years and over                                  | 0             | 0       | 0     |
| Age Continuous                                     |               |         |       |
| Units: Weeks                                       |               |         |       |
| arithmetic mean                                    | 8.6           | 8.6     | -     |
| standard deviation                                 | ± 1.17        | ± 1.24  | -     |
| Sex: Female, Male                                  |               |         |       |
| Units: Participants                                |               |         |       |
| Female                                             | 105           | 135     | 240   |
| Male                                               | 144           | 116     | 260   |
| Race/Ethnicity, Customized                         |               |         |       |
| Units: Subjects                                    |               |         |       |
| Black or African American                          | 1             | 2       | 3     |
| American Indian or Alaska Native                   | 1             | 2       | 3     |
| Asian - Central / South Asian Heritage             | 0             | 1       | 1     |
| Asian - East Asian Heritage                        | 1             | 0       | 1     |
| Asian - South East Asian Heritage                  | 0             | 1       | 1     |
| White - Arabic / North African Heritage            | 5             | 4       | 9     |
| White - Caucasian / European Heritage              | 236           | 235     | 471   |
| Other-Unspecified                                  | 5             | 6       | 11    |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                       |               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| Reporting group title                                                                                                                                                                                                                                 | Infanrix Hexa |
| Reporting group description:<br>All subjects in this group received 3 doses (2 primary doses and 1 booster dose) of DTPa-HBV-IPV/Hib vaccine co-administered with 3 doses of pneumococcal 13 valent conjugate vaccine at 2, 4, and 12 months of age.  |               |
| Reporting group title                                                                                                                                                                                                                                 | Vaxelis       |
| Reporting group description:<br>All subjects in this group received 3 doses (2 primary doses and 1 booster dose) of DTaP5 HBV IPV Hib vaccine co-administered with 3 doses of pneumococcal 13 valent conjugate vaccine at 2, 4, and 12 months of age. |               |

### Primary: Anti-polyribosylribitol phosphate (anti-PRP) antibody concentrations at Month 11, based on Per protocol set (PPS)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Anti-polyribosylribitol phosphate (anti-PRP) antibody concentrations at Month 11, based on Per protocol set (PPS) |
| End point description:<br>Anti-PRP antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in microgram per milliliter ( $\mu\text{g/mL}$ ), as assessed by Enzyme-linked immunosorbent assay (ELISA).<br>The analysis was performed on the Per Protocol Set (PPS), which included all eligible subjects who received diphtheria, tetanus and acellular pertussis (DTPa)-combination study vaccines as per protocol, who had anti-PRP results post-vaccination, who complied with vaccination/blood draw intervals, without intercurrent conditions and without prohibited concomitant medication/vaccination.<br>As specified in Statistical Analysis Plan, only geometric mean was calculated for anti-PRP antibody concentration and was adjusted for DTPa vaccination of the mother. Due to system limitation, "Number" is selected as Measure type instead of "Geometric mean". |                                                                                                                   |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Primary                                                                                                           |
| End point timeframe:<br>At Month 11 (i.e., 1-month post-booster vaccination)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                   |

| End point values            | Infanrix Hexa   | Vaxelis         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 211             | 218             |  |  |
| Units: $\mu\text{g/mL}$     |                 |                 |  |  |
| number (not applicable)     | 11.61           | 12.66           |  |  |

### Statistical analyses

|                                                                                                                                                                                                               |                                             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|
| Statistical analysis title                                                                                                                                                                                    | Non-inferiority of Infanrix Hexa vs Vaxelis |
| Statistical analysis description:<br>Non-inferiority was demonstrated if the lower limit (LL) of the 2sided 95% confidence interval (CI) on group GMC ratio (Infanrix Hexa over Vaxelis group) was above 0.5. |                                             |
| Comparison groups                                                                                                                                                                                             | Infanrix Hexa v Vaxelis                     |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 429                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[1]</sup> |
| Parameter estimate                      | Adjusted GMC Ratio             |
| Point estimate                          | 0.917                          |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 0.71                           |
| upper limit                             | 1.185                          |

Notes:

[1] - The 95% CI for GMC ratio derived from an ANOVA model on log10 transformed concentration was used. GMC was adjusted for DTPA vaccination of the mother.

### **Primary: Percentage of subjects with anti-PRP antibody concentrations equal to or above ( $\geq$ ) 5 µg/mL at Month 11, based on PPS**

|                 |                                                                                                                             |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of subjects with anti-PRP antibody concentrations equal to or above ( $\geq$ ) 5 µg/mL at Month 11, based on PPS |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|

End point description:

The percentage of subjects with anti-PRP antibody concentrations  $\geq$ 5 µg/mL was reported, as assessed by ELISA.

The analysis was performed on PPS, which included all eligible subjects who received all DTPa-combination study vaccines as per protocol, who had anti-PRP results post-vaccination, who complied with vaccination/blood draw intervals, without intercurrent conditions and without prohibited concomitant medication/vaccination.

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

End point timeframe:

At Month 11 (i.e., 1-month post-booster vaccination)

| <b>End point values</b>           | Infanrix Hexa   | Vaxelis         |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 211             | 218             |  |  |
| Units: Percentage of Participants |                 |                 |  |  |
| number (not applicable)           | 75.4            | 81.7            |  |  |

### **Statistical analyses**

|                                   |                                             |
|-----------------------------------|---------------------------------------------|
| <b>Statistical analysis title</b> | Non-inferiority of Infanrix Hexa vs Vaxelis |
|-----------------------------------|---------------------------------------------|

Statistical analysis description:

Non-inferiority was demonstrated if the non inferiority of anti-PRP GMC ratio was met and the LL of the 2 sided 95% CI on group difference in the percentage (Infanrix Hexa over Vaxelis group) was more than -10%.

|                   |                         |
|-------------------|-------------------------|
| Comparison groups | Infanrix Hexa v Vaxelis |
|-------------------|-------------------------|



|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 429                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[2]</sup> |
| Parameter estimate                      | Difference in Percentage       |
| Point estimate                          | -6.3                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -14.1                          |
| upper limit                             | 1.49                           |

Notes:

[2] - The 2 sided 95% CI of group difference in seroconversion rate (Inv\_group minus Com\_group) was computed based on Miettinen and Nurminen method.

### **Primary: Anti-PRP antibody concentrations at Month 11, based on the Exposed Set (ES)**

|                 |                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Anti-PRP antibody concentrations at Month 11, based on the Exposed Set (ES) <sup>[3]</sup> |
|-----------------|--------------------------------------------------------------------------------------------|

End point description:

Anti-PRP antibody concentrations were presented as GMCs and expressed in µg/mL, as assessed by ELISA.

The analysis was performed on the Exposed Set (ES), which included all vaccinated subjects who were analysed according to the intervention they receive at Dose 1.

Only geometric mean was calculated for anti-PRP antibody concentration. Due to system limitation, "Number" is selected as Measure type instead of "Geometric mean".

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

End point timeframe:

At Month 11 (i.e., 1-month post-booster vaccination)

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| <b>End point values</b>     | Infanrix Hexa   | Vaxelis         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 175             | 228             |  |  |
| Units: µg/mL                |                 |                 |  |  |
| number (not applicable)     | 11.26           | 12.85           |  |  |

### **Statistical analyses**

No statistical analyses for this end point

### **Primary: Percentage of subjects with anti-PRP antibody concentrations ≥ 5 µg/mL at Month 11, based on ES**

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of subjects with anti-PRP antibody concentrations ≥ 5 µg/mL at Month 11, based on ES <sup>[4]</sup> |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

The percentage of subjects with anti-PRP antibody concentrations ≥ 5 µg/mL was reported, as assessed by ELISA.

The analysis was performed on the ES, which included all vaccinated subjects who were analysed according to the intervention they receive at Dose 1.

|                                                                                                                                                                     |         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| End point type                                                                                                                                                      | Primary |
| End point timeframe:                                                                                                                                                |         |
| At Month 11 (i.e., 1-month post-booster vaccination)                                                                                                                |         |
| 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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.                                              |         |

| End point values                  | Infanrix Hexa   | Vaxelis         |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 175             | 186             |  |  |
| Units: Percentage of Participants |                 |                 |  |  |
| number (not applicable)           | 75.4            | 81.6            |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of subjects with anti-PRP antibody concentration $\geq 0.15$ $\mu\text{g/mL}$

|                 |                                                                                          |
|-----------------|------------------------------------------------------------------------------------------|
| End point title | Percentage of subjects with anti-PRP antibody concentration $\geq 0.15$ $\mu\text{g/mL}$ |
|-----------------|------------------------------------------------------------------------------------------|

End point description:

The percentage of subjects with anti-PRP antibody concentration equal to or above the threshold for short-term protection was reported. The threshold for short-term protection is 0.15  $\mu\text{g/mL}$ . The analysis was performed on PPS, which included all eligible subjects who received all DTPa-combination study vaccines as per protocol, who had anti-PRP results post-vaccination, who complied with vaccination/blood draw intervals, without intercurrent conditions and without prohibited concomitant medication/vaccination.

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

End point timeframe:

At Month 3 (i.e., 1-month post-primary vaccination), Month 10 (i.e., pre-booster) and Month 11 (i.e., 1-month post-booster vaccination)

| End point values                  | Infanrix Hexa         | Vaxelis               |  |  |
|-----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed       | 213                   | 230                   |  |  |
| Units: Percentage of Participants |                       |                       |  |  |
| number (confidence interval 95%)  |                       |                       |  |  |
| At month 3 (N=213;230)            | 79.8 (73.79 to 84.99) | 100 (98.41 to 100)    |  |  |
| At Month 10 (N=206;216)           | 61.2 (54.14 to 67.86) | 94.4 (90.50 to 97.10) |  |  |
| At Month 11 (N=211;218)           | 99.5 (97.39 to 99.99) | 99.5 (97.47 to 99.99) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with anti-PRP antibody concentrations $\geq 1.0$ $\mu\text{g/mL}$

|                 |                                                                                          |
|-----------------|------------------------------------------------------------------------------------------|
| End point title | Percentage of subjects with anti-PRP antibody concentrations $\geq 1.0$ $\mu\text{g/mL}$ |
|-----------------|------------------------------------------------------------------------------------------|

End point description:

The percentage of subjects with anti-PRP antibody concentration equal to or above the threshold for long-term protection was reported. The threshold for long-term protection is  $1.0$   $\mu\text{g/mL}$ . The analysis was performed on PPS, which included all eligible subjects who received all DTPa-combination study vaccines as per protocol, who had anti-PRP results post-vaccination, who complied with vaccination/blood draw intervals, without intercurrent conditions and without prohibited concomitant medication/vaccination.

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

End point timeframe:

At Month 3 (i.e., 1-month post-primary vaccination), Month 10 (i.e., pre-booster) and Month 11 (i.e., 1-month post-booster vaccination)

| End point values                  | Infanrix Hexa         | Vaxelis               |  |  |
|-----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed       | 213                   | 230                   |  |  |
| Units: Percentage of Participants |                       |                       |  |  |
| number (confidence interval 95%)  |                       |                       |  |  |
| At Month 3 (N=213;230)            | 30.5 (24.41 to 37.18) | 92.2 (87.91 to 95.30) |  |  |
| At Month 10 (N=206;216)           | 13.1 (8.82 to 18.49)  | 69.0 (62.35 to 75.08) |  |  |
| At Month 11 (N=211;218)           | 97.2 (93.91 to 98.95) | 94.5 (90.58 to 97.12) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-PRP antibody concentrations

|                 |                                  |
|-----------------|----------------------------------|
| End point title | Anti-PRP antibody concentrations |
|-----------------|----------------------------------|

End point description:

Anti-PRP antibody concentrations were presented as GMCs and expressed in  $\mu\text{g/mL}$ , as assessed by ELISA.

The analysis was performed on PPS, which included all eligible subjects who received all DTPa-combination study vaccines as per protocol, who had anti-PRP results post-vaccination, who complied with vaccination/blood draw intervals, without intercurrent conditions and without prohibited concomitant medication/vaccination.

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

End point timeframe:

At Month 3 (i.e., 1-month post-primary vaccination), Month 10 (i.e., pre-booster) and Month 11 (i.e., 1-month post-booster vaccination)

| End point values                         | Infanrix Hexa        | Vaxelis               |  |  |
|------------------------------------------|----------------------|-----------------------|--|--|
| Subject group type                       | Reporting group      | Reporting group       |  |  |
| Number of subjects analysed              | 213                  | 230                   |  |  |
| Units: µg/mL                             |                      |                       |  |  |
| geometric mean (confidence interval 95%) |                      |                       |  |  |
| At Month 3 (N=213;230)                   | 0.5 (0.41 to 0.62)   | 11.3 (9.35 to 13.60)  |  |  |
| At Month 10 (N=206;216)                  | 0.2 (0.19 to 0.28)   | 1.9 (1.56 to 2.26)    |  |  |
| At Month 11 (N=211;218)                  | 12.0 (9.96 to 14.34) | 12.9 (10.75 to 15.55) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with unsolicited adverse events (AEs)

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | Number of subjects with unsolicited adverse events (AEs) |
|-----------------|----------------------------------------------------------|

End point description:

AEs are defined as any untoward medical occurrence in a subject or subjects, temporally associated with the use of study treatment, whether or not considered related to the study treatment.

The analysis was performed on the ES, which included all vaccinated subjects who were analysed according to the intervention they receive at Dose 1.

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

End point timeframe:

During the 31-day (Days 1-31) follow-up period after each vaccination (vaccines administered at 2, 4 and 12 months of age)

| End point values            | Infanrix Hexa   | Vaxelis         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 249             | 251             |  |  |
| Units: Participants         | 178             | 199             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with serious adverse events (SAEs)

|                 |                                                       |
|-----------------|-------------------------------------------------------|
| End point title | Number of subjects with serious adverse events (SAEs) |
|-----------------|-------------------------------------------------------|

End point description:

An SAEs is defined as any untoward medical occurrence that, at any dose, result in death, is life-

threatening, requires inpatient hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect.

The analysis was performed on the ES, which included all vaccinated subjects who were analysed according to the intervention they receive at Dose 1.

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

End point timeframe:

During the 31-day (Days 1-31) follow-up period after each vaccination (vaccines administered at 2, 4 and 12 months of age)

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>     | Infanrix Hexa   | Vaxelis         |  |  |
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 249             | 251             |  |  |
| Units: Participants         | 14              | 10              |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events (SAEs) were collected throughout the entire period of the study (from Day 1 up to study end [Month 11]). Non Serious AEs (Other AEs) were collected 31 days after each vaccination (vaccines administered at 2, 4 and 12 months of age).

Adverse event reporting additional description:

As number of occurrences of SAEs was not collected, number of subjects affected was reported instead.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Vaxelis |
|-----------------------|---------|

Reporting group description:

All subjects in this group received 3 doses (2 primary doses and 1 booster dose) of DTaP5 HBV IPV Hib vaccine co-administered with 3 doses of pneumococcal 13 valent conjugate vaccine at 2, 4, and 12 months of age.

|                       |               |
|-----------------------|---------------|
| Reporting group title | Infanrix Hexa |
|-----------------------|---------------|

Reporting group description:

All subjects in this group received 3 doses (2 primary doses and 1 booster dose) of DTPa-HBV-IPV/Hib vaccine co-administered with 3 doses of pneumococcal 13 valent conjugate vaccine at 2, 4, and 12 months of age.

| Serious adverse events                            | Vaxelis          | Infanrix Hexa    |  |
|---------------------------------------------------|------------------|------------------|--|
| Total subjects affected by serious adverse events |                  |                  |  |
| subjects affected / exposed                       | 10 / 251 (3.98%) | 14 / 249 (5.62%) |  |
| number of deaths (all causes)                     | 0                | 0                |  |
| number of deaths resulting from adverse events    | 0                | 0                |  |
| Investigations                                    |                  |                  |  |
| Enterovirus test positive                         |                  |                  |  |
| subjects affected / exposed                       | 0 / 251 (0.00%)  | 1 / 249 (0.40%)  |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Congenital, familial and genetic disorders        |                  |                  |  |
| Hydrocele                                         |                  |                  |  |
| subjects affected / exposed                       | 0 / 251 (0.00%)  | 1 / 249 (0.40%)  |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Nervous system disorders                          |                  |                  |  |
| Seizure                                           |                  |                  |  |

|                                                      |                 |                 |  |
|------------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 251 (0.00%) | 2 / 249 (0.80%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 1 / 2           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Febrile convulsion                                   |                 |                 |  |
| subjects affected / exposed                          | 1 / 251 (0.40%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Pyrexia                                              |                 |                 |  |
| subjects affected / exposed                          | 0 / 251 (0.00%) | 2 / 249 (0.80%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                           |                 |                 |  |
| Vomiting                                             |                 |                 |  |
| subjects affected / exposed                          | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Diarrhoea                                            |                 |                 |  |
| subjects affected / exposed                          | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Reproductive system and breast disorders             |                 |                 |  |
| Testicular torsion                                   |                 |                 |  |
| subjects affected / exposed                          | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders      |                 |                 |  |
| Respiratory failure                                  |                 |                 |  |
| subjects affected / exposed                          | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Infections and infestations                          |                 |                 |  |
| Abscess neck                                         |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Adenovirus infection                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchiolitis                                   |                 |                 |  |
| subjects affected / exposed                     | 3 / 251 (1.20%) | 2 / 249 (0.80%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchitis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Parainfluenzae virus infection                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis norovirus                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 251 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Perirectal abscess                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory syncytial virus bronchiolitis       |                 |                 |  |



|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 3 / 251 (1.20%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pyelonephritis acute                            |                 |                 |  |
| subjects affected / exposed                     | 2 / 251 (0.80%) | 0 / 249 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Rhinovirus infection                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 251 (0.00%) | 2 / 249 (0.80%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Hypophagia                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| 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: 0 %

| Non-serious adverse events                                          | Vaxelis            | Infanrix Hexa      |  |
|---------------------------------------------------------------------|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events               |                    |                    |  |
| subjects affected / exposed                                         | 199 / 251 (79.28%) | 178 / 249 (71.49%) |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                    |  |
| Melanocytic naevus                                                  |                    |                    |  |
| subjects affected / exposed                                         | 1 / 251 (0.40%)    | 0 / 249 (0.00%)    |  |
| occurrences (all)                                                   | 1                  | 0                  |  |

|                                                                                                                                                |                      |                      |  |
|------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| Haemangioma of skin<br>subjects affected / exposed<br>occurrences (all)                                                                        | 1 / 251 (0.40%)<br>1 | 2 / 249 (0.80%)<br>2 |  |
| Vascular disorders<br>Pallor<br>subjects affected / exposed<br>occurrences (all)                                                               | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1 |  |
| General disorders and administration<br>site conditions<br>Administration site haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Administration site pain<br>subjects affected / exposed<br>occurrences (all)                                                                   | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Induration<br>subjects affected / exposed<br>occurrences (all)                                                                                 | 1 / 251 (0.40%)<br>1 | 1 / 249 (0.40%)<br>1 |  |
| Discomfort<br>subjects affected / exposed<br>occurrences (all)                                                                                 | 4 / 251 (1.59%)<br>4 | 2 / 249 (0.80%)<br>2 |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                                                                                    | 3 / 251 (1.20%)<br>4 | 2 / 249 (0.80%)<br>2 |  |
| Hyperpyrexia<br>subjects affected / exposed<br>occurrences (all)                                                                               | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Crying<br>subjects affected / exposed<br>occurrences (all)                                                                                     | 7 / 251 (2.79%)<br>7 | 5 / 249 (2.01%)<br>5 |  |
| Inflammation<br>subjects affected / exposed<br>occurrences (all)                                                                               | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Injection site discomfort<br>subjects affected / exposed<br>occurrences (all)                                                                  | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Injection site erythema                                                                                                                        |                      |                      |  |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 8 / 251 (3.19%) | 6 / 249 (2.41%) |
| occurrences (all)           | 9               | 8               |
| Injection site haemorrhage  |                 |                 |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |
| occurrences (all)           | 0               | 1               |
| Injection site induration   |                 |                 |
| subjects affected / exposed | 0 / 251 (0.00%) | 3 / 249 (1.20%) |
| occurrences (all)           | 0               | 3               |
| Malaise                     |                 |                 |
| subjects affected / exposed | 3 / 251 (1.20%) | 2 / 249 (0.80%) |
| occurrences (all)           | 3               | 3               |
| Injection site pain         |                 |                 |
| subjects affected / exposed | 8 / 251 (3.19%) | 6 / 249 (2.41%) |
| occurrences (all)           | 8               | 7               |
| Injection site swelling     |                 |                 |
| subjects affected / exposed | 8 / 251 (3.19%) | 7 / 249 (2.81%) |
| occurrences (all)           | 11              | 8               |
| Injection site warmth       |                 |                 |
| subjects affected / exposed | 2 / 251 (0.80%) | 0 / 249 (0.00%) |
| occurrences (all)           | 2               | 0               |
| Irritability postvaccinal   |                 |                 |
| subjects affected / exposed | 1 / 251 (0.40%) | 1 / 249 (0.40%) |
| occurrences (all)           | 1               | 1               |
| Injection site oedema       |                 |                 |
| subjects affected / exposed | 2 / 251 (0.80%) | 0 / 249 (0.00%) |
| occurrences (all)           | 2               | 0               |
| Nodule                      |                 |                 |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 249 (0.00%) |
| occurrences (all)           | 1               | 0               |
| Pain                        |                 |                 |
| subjects affected / exposed | 2 / 251 (0.80%) | 1 / 249 (0.40%) |
| occurrences (all)           | 3               | 1               |
| Peripheral swelling         |                 |                 |
| subjects affected / exposed | 4 / 251 (1.59%) | 4 / 249 (1.61%) |
| occurrences (all)           | 4               | 4               |
| Pyrexia                     |                 |                 |

|                                                                                                                          |                           |                           |  |
|--------------------------------------------------------------------------------------------------------------------------|---------------------------|---------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                         | 132 / 251 (52.59%)<br>237 | 103 / 249 (41.37%)<br>181 |  |
| Swelling<br>subjects affected / exposed<br>occurrences (all)                                                             | 1 / 251 (0.40%)<br>1      | 1 / 249 (0.40%)<br>1      |  |
| Vaccination site granuloma<br>subjects affected / exposed<br>occurrences (all)                                           | 1 / 251 (0.40%)<br>2      | 0 / 249 (0.00%)<br>0      |  |
| Vaccination site induration<br>subjects affected / exposed<br>occurrences (all)                                          | 2 / 251 (0.80%)<br>2      | 0 / 249 (0.00%)<br>0      |  |
| Vaccination site swelling<br>subjects affected / exposed<br>occurrences (all)                                            | 1 / 251 (0.40%)<br>1      | 0 / 249 (0.00%)<br>0      |  |
| Vaccination site erythema<br>subjects affected / exposed<br>occurrences (all)                                            | 2 / 251 (0.80%)<br>2      | 0 / 249 (0.00%)<br>0      |  |
| Immune system disorders<br>Food allergy<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 251 (0.40%)<br>1      | 0 / 249 (0.00%)<br>0      |  |
| Allergy to arthropod bite<br>subjects affected / exposed<br>occurrences (all)                                            | 1 / 251 (0.40%)<br>1      | 0 / 249 (0.00%)<br>0      |  |
| Milk allergy<br>subjects affected / exposed<br>occurrences (all)                                                         | 3 / 251 (1.20%)<br>3      | 0 / 249 (0.00%)<br>0      |  |
| Reproductive system and breast disorders<br>Genital labial adhesions<br>subjects affected / exposed<br>occurrences (all) | 2 / 251 (0.80%)<br>2      | 2 / 249 (0.80%)<br>2      |  |
| Respiratory, thoracic and mediastinal disorders<br>Catarrh<br>subjects affected / exposed<br>occurrences (all)           | 1 / 251 (0.40%)<br>1      | 0 / 249 (0.00%)<br>0      |  |
| Bronchospasm                                                                                                             |                           |                           |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 251 (0.80%) | 0 / 249 (0.00%) |  |
| occurrences (all)           | 2               | 0               |  |
| Bronchial hyperreactivity   |                 |                 |  |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Cough                       |                 |                 |  |
| subjects affected / exposed | 5 / 251 (1.99%) | 7 / 249 (2.81%) |  |
| occurrences (all)           | 6               | 8               |  |
| Nasal congestion            |                 |                 |  |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Pharyngeal inflammation     |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Respiratory disorder        |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Rhinorrhoea                 |                 |                 |  |
| subjects affected / exposed | 4 / 251 (1.59%) | 0 / 249 (0.00%) |  |
| occurrences (all)           | 4               | 0               |  |
| Psychiatric disorders       |                 |                 |  |
| Depressed mood              |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Anxiety                     |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Agitation                   |                 |                 |  |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Insomnia                    |                 |                 |  |
| subjects affected / exposed | 2 / 251 (0.80%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 2               | 1               |  |
| Sleep disorder              |                 |                 |  |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |

|                                                                                     |                         |                         |  |
|-------------------------------------------------------------------------------------|-------------------------|-------------------------|--|
| Restlessness<br>subjects affected / exposed<br>occurrences (all)                    | 13 / 251 (5.18%)<br>18  | 8 / 249 (3.21%)<br>14   |  |
| Irritability<br>subjects affected / exposed<br>occurrences (all)                    | 37 / 251 (14.74%)<br>56 | 31 / 249 (12.45%)<br>48 |  |
| Investigations                                                                      |                         |                         |  |
| Body temperature increased<br>subjects affected / exposed<br>occurrences (all)      | 5 / 251 (1.99%)<br>5    | 3 / 249 (1.20%)<br>3    |  |
| Body temperature decreased<br>subjects affected / exposed<br>occurrences (all)      | 1 / 251 (0.40%)<br>1    | 0 / 249 (0.00%)<br>0    |  |
| Blood iron decreased<br>subjects affected / exposed<br>occurrences (all)            | 2 / 251 (0.80%)<br>2    | 1 / 249 (0.40%)<br>1    |  |
| Injury, poisoning and procedural complications                                      |                         |                         |  |
| Arthropod bite<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 251 (0.80%)<br>2    | 1 / 249 (0.40%)<br>1    |  |
| Bite<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 251 (0.00%)<br>0    | 1 / 249 (0.40%)<br>1    |  |
| Face injury<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 251 (0.00%)<br>0    | 2 / 249 (0.80%)<br>2    |  |
| Eye injury<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 251 (0.40%)<br>1    | 0 / 249 (0.00%)<br>0    |  |
| Vascular procedure complication<br>subjects affected / exposed<br>occurrences (all) | 1 / 251 (0.40%)<br>1    | 0 / 249 (0.00%)<br>0    |  |
| Tibia fracture<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 251 (0.00%)<br>0    | 1 / 249 (0.40%)<br>1    |  |
| Nasal injury                                                                        |                         |                         |  |

|                                                                                                                               |                      |                      |  |
|-------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                              | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1 |  |
| Head injury<br>subjects affected / exposed<br>occurrences (all)                                                               | 1 / 251 (0.40%)<br>1 | 2 / 249 (0.80%)<br>2 |  |
| Hair-thread tourniquet syndrome<br>subjects affected / exposed<br>occurrences (all)                                           | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Electric shock<br>subjects affected / exposed<br>occurrences (all)                                                            | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Congenital, familial and genetic disorders<br>Developmental hip dysplasia<br>subjects affected / exposed<br>occurrences (all) | 2 / 251 (0.80%)<br>2 | 0 / 249 (0.00%)<br>0 |  |
| Ankyloglossia congenital<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1 |  |
| Odontogenic cyst<br>subjects affected / exposed<br>occurrences (all)                                                          | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Microcephaly<br>subjects affected / exposed<br>occurrences (all)                                                              | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Plagiocephaly<br>subjects affected / exposed<br>occurrences (all)                                                             | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Cardiac disorders<br>Pulmonary valve stenosis<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Nervous system disorders<br>Somnolence<br>subjects affected / exposed<br>occurrences (all)                                    | 5 / 251 (1.99%)<br>5 | 4 / 249 (1.61%)<br>4 |  |
| Hypertonia                                                                                                                    |                      |                      |  |

|                                                                                                                     |                      |                      |  |
|---------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                    | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1 |  |
| Head titubation<br>subjects affected / exposed<br>occurrences (all)                                                 | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Syncope<br>subjects affected / exposed<br>occurrences (all)                                                         | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1 |  |
| Blood and lymphatic system disorders<br>Iron deficiency anaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)                                                 | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1 |  |
| Thrombocytosis<br>subjects affected / exposed<br>occurrences (all)                                                  | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1 |  |
| Ear and labyrinth disorders<br>Otorrhoea<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Eye disorders<br>Astigmatism<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1 |  |
| Corneal erosion<br>subjects affected / exposed<br>occurrences (all)                                                 | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0 |  |
| Dacryostenosis acquired<br>subjects affected / exposed<br>occurrences (all)                                         | 1 / 251 (0.40%)<br>1 | 3 / 249 (1.20%)<br>3 |  |
| Hypermetropia<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1 |  |
| Eye irritation                                                                                                      |                      |                      |  |



|                             |                  |                  |  |
|-----------------------------|------------------|------------------|--|
| subjects affected / exposed | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences (all)           | 1                | 0                |  |
| Eye haematoma               |                  |                  |  |
| subjects affected / exposed | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences (all)           | 1                | 0                |  |
| Gastrointestinal disorders  |                  |                  |  |
| Abdominal distension        |                  |                  |  |
| subjects affected / exposed | 0 / 251 (0.00%)  | 1 / 249 (0.40%)  |  |
| occurrences (all)           | 0                | 1                |  |
| Abdominal pain              |                  |                  |  |
| subjects affected / exposed | 4 / 251 (1.59%)  | 6 / 249 (2.41%)  |  |
| occurrences (all)           | 4                | 6                |  |
| Abdominal pain upper        |                  |                  |  |
| subjects affected / exposed | 0 / 251 (0.00%)  | 1 / 249 (0.40%)  |  |
| occurrences (all)           | 0                | 1                |  |
| Diarrhoea                   |                  |                  |  |
| subjects affected / exposed | 16 / 251 (6.37%) | 15 / 249 (6.02%) |  |
| occurrences (all)           | 19               | 20               |  |
| Anal fissure                |                  |                  |  |
| subjects affected / exposed | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences (all)           | 1                | 0                |  |
| Constipation                |                  |                  |  |
| subjects affected / exposed | 9 / 251 (3.59%)  | 3 / 249 (1.20%)  |  |
| occurrences (all)           | 10               | 3                |  |
| Dental cyst                 |                  |                  |  |
| subjects affected / exposed | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences (all)           | 1                | 0                |  |
| Anal erythema               |                  |                  |  |
| subjects affected / exposed | 0 / 251 (0.00%)  | 1 / 249 (0.40%)  |  |
| occurrences (all)           | 0                | 1                |  |
| Dry mouth                   |                  |                  |  |
| subjects affected / exposed | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences (all)           | 1                | 0                |  |
| Flatulence                  |                  |                  |  |
| subjects affected / exposed | 4 / 251 (1.59%)  | 2 / 249 (0.80%)  |  |
| occurrences (all)           | 4                | 2                |  |

|                                                                                      |                      |                       |  |
|--------------------------------------------------------------------------------------|----------------------|-----------------------|--|
| Frequent bowel movements<br>subjects affected / exposed<br>occurrences (all)         | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1  |  |
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all) | 4 / 251 (1.59%)<br>4 | 6 / 249 (2.41%)<br>6  |  |
| Regurgitation<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0  |  |
| Infantile colic<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 251 (0.80%)<br>2 | 3 / 249 (1.20%)<br>3  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1  |  |
| Odynophagia<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1  |  |
| Oral pain<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1  |  |
| Haematochezia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 251 (0.00%)<br>0 | 2 / 249 (0.80%)<br>2  |  |
| Teething<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 251 (0.40%)<br>2 | 3 / 249 (1.20%)<br>4  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                         | 5 / 251 (1.99%)<br>5 | 8 / 249 (3.21%)<br>10 |  |
| Skin and subcutaneous tissue disorders                                               |                      |                       |  |
| Erythema<br>subjects affected / exposed<br>occurrences (all)                         | 3 / 251 (1.20%)<br>3 | 2 / 249 (0.80%)<br>2  |  |
| Papule                                                                               |                      |                       |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Eczema                      |                 |                 |  |
| subjects affected / exposed | 5 / 251 (1.99%) | 6 / 249 (2.41%) |  |
| occurrences (all)           | 5               | 7               |  |
| Dry skin                    |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Dermatitis diaper           |                 |                 |  |
| subjects affected / exposed | 6 / 251 (2.39%) | 6 / 249 (2.41%) |  |
| occurrences (all)           | 7               | 6               |  |
| Dermatitis atopic           |                 |                 |  |
| subjects affected / exposed | 1 / 251 (0.40%) | 3 / 249 (1.20%) |  |
| occurrences (all)           | 1               | 3               |  |
| Dermatitis                  |                 |                 |  |
| subjects affected / exposed | 4 / 251 (1.59%) | 7 / 249 (2.81%) |  |
| occurrences (all)           | 4               | 7               |  |
| Rash pruritic               |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Seborrhoeic dermatitis      |                 |                 |  |
| subjects affected / exposed | 1 / 251 (0.40%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 1               | 1               |  |
| Skin mass                   |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Urticaria                   |                 |                 |  |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Rash                        |                 |                 |  |
| subjects affected / exposed | 3 / 251 (1.20%) | 5 / 249 (2.01%) |  |
| occurrences (all)           | 3               | 5               |  |
| Rash macular                |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Renal and urinary disorders |                 |                 |  |

|                                                                           |                      |                        |  |
|---------------------------------------------------------------------------|----------------------|------------------------|--|
| Chromaturia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1   |  |
| Musculoskeletal and connective tissue disorders                           |                      |                        |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)     | 2 / 251 (0.80%)<br>2 | 0 / 249 (0.00%)<br>0   |  |
| Torticollis<br>subjects affected / exposed<br>occurrences (all)           | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1   |  |
| Infections and infestations                                               |                      |                        |  |
| Acarodermatitis<br>subjects affected / exposed<br>occurrences (all)       | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1   |  |
| Asymptomatic COVID-19<br>subjects affected / exposed<br>occurrences (all) | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1   |  |
| Bronchiolitis<br>subjects affected / exposed<br>occurrences (all)         | 3 / 251 (1.20%)<br>3 | 4 / 249 (1.61%)<br>4   |  |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)            | 5 / 251 (1.99%)<br>5 | 6 / 249 (2.41%)<br>7   |  |
| Candida nappy rash<br>subjects affected / exposed<br>occurrences (all)    | 2 / 251 (0.80%)<br>2 | 2 / 249 (0.80%)<br>2   |  |
| Fungal skin infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 251 (0.00%)<br>0 | 1 / 249 (0.40%)<br>1   |  |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)              | 9 / 251 (3.59%)<br>9 | 14 / 249 (5.62%)<br>14 |  |
| Croup infectious<br>subjects affected / exposed<br>occurrences (all)      | 1 / 251 (0.40%)<br>1 | 0 / 249 (0.00%)<br>0   |  |
| Ear infection                                                             |                      |                        |  |

|                                     |                  |                  |
|-------------------------------------|------------------|------------------|
| subjects affected / exposed         | 1 / 251 (0.40%)  | 2 / 249 (0.80%)  |
| occurrences (all)                   | 1                | 2                |
| Escherichia urinary tract infection |                  |                  |
| subjects affected / exposed         | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |
| occurrences (all)                   | 1                | 0                |
| Exanthema subitum                   |                  |                  |
| subjects affected / exposed         | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |
| occurrences (all)                   | 1                | 0                |
| Conjunctivitis                      |                  |                  |
| subjects affected / exposed         | 14 / 251 (5.58%) | 14 / 249 (5.62%) |
| occurrences (all)                   | 15               | 14               |
| Gastroenteritis                     |                  |                  |
| subjects affected / exposed         | 10 / 251 (3.98%) | 9 / 249 (3.61%)  |
| occurrences (all)                   | 11               | 9                |
| Hand-foot-and-mouth disease         |                  |                  |
| subjects affected / exposed         | 2 / 251 (0.80%)  | 2 / 249 (0.80%)  |
| occurrences (all)                   | 2                | 2                |
| Herpangina                          |                  |                  |
| subjects affected / exposed         | 2 / 251 (0.80%)  | 1 / 249 (0.40%)  |
| occurrences (all)                   | 2                | 1                |
| Impetigo                            |                  |                  |
| subjects affected / exposed         | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |
| occurrences (all)                   | 1                | 0                |
| Infected fistula                    |                  |                  |
| subjects affected / exposed         | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |
| occurrences (all)                   | 1                | 0                |
| Influenza                           |                  |                  |
| subjects affected / exposed         | 0 / 251 (0.00%)  | 2 / 249 (0.80%)  |
| occurrences (all)                   | 0                | 2                |
| Laryngitis                          |                  |                  |
| subjects affected / exposed         | 4 / 251 (1.59%)  | 5 / 249 (2.01%)  |
| occurrences (all)                   | 4                | 5                |
| Nasopharyngitis                     |                  |                  |
| subjects affected / exposed         | 14 / 251 (5.58%) | 6 / 249 (2.41%)  |
| occurrences (all)                   | 14               | 7                |
| Oral candidiasis                    |                  |                  |

|                                       |                 |                 |
|---------------------------------------|-----------------|-----------------|
| subjects affected / exposed           | 5 / 251 (1.99%) | 4 / 249 (1.61%) |
| occurrences (all)                     | 5               | 4               |
| Otitis media                          |                 |                 |
| subjects affected / exposed           | 0 / 251 (0.00%) | 1 / 249 (0.40%) |
| occurrences (all)                     | 0               | 1               |
| Otitis media acute                    |                 |                 |
| subjects affected / exposed           | 6 / 251 (2.39%) | 5 / 249 (2.01%) |
| occurrences (all)                     | 6               | 5               |
| Paronychia                            |                 |                 |
| subjects affected / exposed           | 1 / 251 (0.40%) | 0 / 249 (0.00%) |
| occurrences (all)                     | 1               | 0               |
| Roseola                               |                 |                 |
| subjects affected / exposed           | 0 / 251 (0.00%) | 1 / 249 (0.40%) |
| occurrences (all)                     | 0               | 1               |
| Rhinitis                              |                 |                 |
| subjects affected / exposed           | 5 / 251 (1.99%) | 2 / 249 (0.80%) |
| occurrences (all)                     | 5               | 2               |
| Respiratory tract infection viral     |                 |                 |
| subjects affected / exposed           | 3 / 251 (1.20%) | 3 / 249 (1.20%) |
| occurrences (all)                     | 3               | 3               |
| Respiratory tract infection           |                 |                 |
| subjects affected / exposed           | 6 / 251 (2.39%) | 2 / 249 (0.80%) |
| occurrences (all)                     | 8               | 2               |
| Respiratory syncytial virus infection |                 |                 |
| subjects affected / exposed           | 1 / 251 (0.40%) | 0 / 249 (0.00%) |
| occurrences (all)                     | 1               | 0               |
| Pyelonephritis                        |                 |                 |
| subjects affected / exposed           | 0 / 251 (0.00%) | 1 / 249 (0.40%) |
| occurrences (all)                     | 0               | 1               |
| Pneumonia                             |                 |                 |
| subjects affected / exposed           | 1 / 251 (0.40%) | 0 / 249 (0.00%) |
| occurrences (all)                     | 1               | 0               |
| Pilonidal disease                     |                 |                 |
| subjects affected / exposed           | 0 / 251 (0.00%) | 1 / 249 (0.40%) |
| occurrences (all)                     | 0               | 1               |
| Pharyngotonsillitis                   |                 |                 |

|                                         |                  |                  |  |
|-----------------------------------------|------------------|------------------|--|
| subjects affected / exposed             | 0 / 251 (0.00%)  | 1 / 249 (0.40%)  |  |
| occurrences (all)                       | 0                | 1                |  |
| Pharyngitis                             |                  |                  |  |
| subjects affected / exposed             | 3 / 251 (1.20%)  | 1 / 249 (0.40%)  |  |
| occurrences (all)                       | 3                | 1                |  |
| Viral upper respiratory tract infection |                  |                  |  |
| subjects affected / exposed             | 6 / 251 (2.39%)  | 5 / 249 (2.01%)  |  |
| occurrences (all)                       | 6                | 6                |  |
| Viral rash                              |                  |                  |  |
| subjects affected / exposed             | 2 / 251 (0.80%)  | 1 / 249 (0.40%)  |  |
| occurrences (all)                       | 2                | 1                |  |
| Viral infection                         |                  |                  |  |
| subjects affected / exposed             | 4 / 251 (1.59%)  | 1 / 249 (0.40%)  |  |
| occurrences (all)                       | 4                | 1                |  |
| Urinary tract infection                 |                  |                  |  |
| subjects affected / exposed             | 3 / 251 (1.20%)  | 1 / 249 (0.40%)  |  |
| occurrences (all)                       | 3                | 1                |  |
| Tonsillitis bacterial                   |                  |                  |  |
| subjects affected / exposed             | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences (all)                       | 1                | 0                |  |
| Tonsillitis                             |                  |                  |  |
| subjects affected / exposed             | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences (all)                       | 1                | 0                |  |
| Suspected COVID-19                      |                  |                  |  |
| subjects affected / exposed             | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences (all)                       | 1                | 0                |  |
| Subglottic laryngitis                   |                  |                  |  |
| subjects affected / exposed             | 1 / 251 (0.40%)  | 0 / 249 (0.00%)  |  |
| occurrences (all)                       | 1                | 0                |  |
| Upper respiratory tract infection       |                  |                  |  |
| subjects affected / exposed             | 20 / 251 (7.97%) | 18 / 249 (7.23%) |  |
| occurrences (all)                       | 24               | 22               |  |
| Metabolism and nutrition disorders      |                  |                  |  |
| Decreased appetite                      |                  |                  |  |
| subjects affected / exposed             | 5 / 251 (1.99%)  | 4 / 249 (1.61%)  |  |
| occurrences (all)                       | 5                | 5                |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| Lactose intolerance         |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |
| Iron deficiency             |                 |                 |  |
| subjects affected / exposed | 1 / 251 (0.40%) | 0 / 249 (0.00%) |  |
| occurrences (all)           | 1               | 0               |  |
| Hypoferritinaemia           |                 |                 |  |
| subjects affected / exposed | 0 / 251 (0.00%) | 1 / 249 (0.40%) |  |
| occurrences (all)           | 0               | 1               |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported