



Clinical trial results:

A phase III, randomized, open-label, multicentre study to assess the immunogenicity, safety and reactogenicity of GlaxoSmithKline Biologicals' combined DTPa-IPV/Hib vaccine administered as a three-dose primary vaccination course at 2-4-6 months of age in healthy infants in South Korea.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2012-004137-16 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 24 February 2012 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 |
| This version publication date | 08 July 2016 |
| First version publication date | 02 July 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Data correction due to a system error in EudraCT – Results |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 114260 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01309646 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330 |
| Public contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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 | 21 March 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 24 February 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 February 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the immunogenicity of GSK Biologicals' DTPa-IPV/Hib vaccine administered at 2, 4 and 6 months of age is non-inferior to that of the concomitant administration of GSK Biologicals' DTPa-IPV and Hib vaccines, in terms of immune response to all vaccine antigens, one month after the third dose of the primary vaccination.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up for one month (minimum 30 days) following administration of the last dose of study vaccines.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 04 March 2011 |
| 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 | Korea, Republic of: 454 |
| Worldwide total number of subjects | 454 |
| EEA total number of subjects | 0 |

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) | 454 |
| 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:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

| | |
|------------------------------|------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Infanrix-IPV+Hib Group |

Arm description:

Subjects aged between, and including, 42 and 69 days at the time of first vaccination received 3 doses of Infanrix-IPV+Hib at 2, 4 and 6 months of age, 3 doses of Synflorix at 6 weeks, 3.5 and 5.5 months of age and 2 doses of Rotarix at 6 weeks and 3.5 months of age. The Infanrix-IPV+Hib was administered intramuscularly in the right thigh, the Synflorix vaccine was administered intramuscularly in the left thigh and the Rotarix vaccine was administered orally.

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

Dosage and administration details:

Intramuscular, 3 doses at 2,4 and 6 months of age.

| | |
|--|--------------------------|
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | 10Pn-PD-DiT |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Intramuscular, 3 doses at 6 weeks, 3.5 and 5.5 months of age.

| | |
|--|--|
| Investigational medicinal product name | Rotarix |
| Investigational medicinal product code | |
| Other name | HRV |
| Pharmaceutical forms | Powder and solvent for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Oral, 2 doses at 6 weeks and 3.5 months of age.

| | |
|------------------|--------------------|
| Arm title | Infanrix IPV Group |
|------------------|--------------------|

Arm description:

Subjects aged between, and including, 42 and 69 days at the time of first vaccination received 3 doses of Infanrix IPV and Hiberix co-administered at separate injection sites at 2, 4 and 6 months of age, 3 dose of Synflorix at 6 weeks, 3.5 and 5.5 months of age and 2 doses of Rotarix at 6 weeks and 3.5 months of age. The Infanrix IPV was administered intramuscularly in the right thigh, the Synflorix and Hiberix vaccines were administered intramuscularly in the left thigh and the Rotarix vaccine was

administered orally.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Infanrix IPV |
| Investigational medicinal product code | |
| Other name | DTPa-IPV |
| Pharmaceutical forms | Powder and suspension for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Intramuscular, 3 doses co-administered at 2, 4 and 6 months of age with Hiberix™.

| | |
|--|---|
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Intramuscular, 3 doses co-administered at 2, 4 and 6 months of age with Infanrix™ IPV.

| | |
|--|--------------------------|
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | 10Pn-PD-DiT |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Intramuscular, 3 doses at 6 weeks, 3.5 and 5.5 months of age.

| | |
|--|--|
| Investigational medicinal product name | Rotarix |
| Investigational medicinal product code | |
| Other name | HRV |
| Pharmaceutical forms | Powder and solvent for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Oral, 2 doses at 6 weeks and 3.5 months of age.

| Number of subjects in period 1 | Infanrix-IPV+Hib Group | Infanrix IPV Group |
|---------------------------------------|------------------------|--------------------|
| Started | 226 | 228 |
| Completed | 224 | 227 |
| Not completed | 2 | 1 |
| Consent withdrawn by subject | 1 | - |
| Protocol Violation | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|------------------------|
| Reporting group title | Infanrix-IPV+Hib Group |
| Reporting group description: | |
| Subjects aged between, and including, 42 and 69 days at the time of first vaccination received 3 doses of Infanrix-IPV+Hib at 2, 4 and 6 months of age, 3 doses of Synflorix at 6 weeks, 3.5 and 5.5 months of age and 2 doses of Rotarix at 6 weeks and 3.5 months of age. The Infanrix-IPV+Hib was administered intramuscularly in the right thigh, the Synflorix vaccine was administered intramuscularly in the left thigh and the Rotarix vaccine was administered orally. | |
| Reporting group title | Infanrix IPV Group |
| Reporting group description: | |
| Subjects aged between, and including, 42 and 69 days at the time of first vaccination received 3 doses of Infanrix IPV and Hiberix co-administered at separate injection sites at 2, 4 and 6 months of age, 3 dose of Synflorix at 6 weeks, 3.5 and 5.5 months of age and 2 doses of Rotarix at 6 weeks and 3.5 months of age. The Infanrix IPV was administered intramuscularly in the right thigh, the Synflorix and Hiberix vaccines were administered intramuscularly in the left thigh and the Rotarix vaccine was administered orally. | |

| Reporting group values | Infanrix-IPV+Hib Group | Infanrix IPV Group | Total |
|--|------------------------|--------------------|-------|
| Number of subjects | 226 | 228 | 454 |
| Age categorical Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous Units: weeks | | | |
| arithmetic mean | 8.8 | 8.8 | |
| standard deviation | ± 1.1 | ± 1.09 | - |
| Gender categorical Units: Subjects | | | |
| Female | 98 | 116 | 214 |
| Male | 128 | 112 | 240 |

End points

End points reporting groups

| | |
|--|------------------------|
| Reporting group title | Infanrix-IPV+Hib Group |
| Reporting group description: | |
| Subjects aged between, and including, 42 and 69 days at the time of first vaccination received 3 doses of Infanrix-IPV+Hib at 2, 4 and 6 months of age, 3 doses of Synflorix at 6 weeks, 3.5 and 5.5 months of age and 2 doses of Rotarix at 6 weeks and 3.5 months of age. The Infanrix-IPV+Hib was administered intramuscularly in the right thigh, the Synflorix vaccine was administered intramuscularly in the left thigh and the Rotarix vaccine was administered orally. | |
| Reporting group title | Infanrix IPV Group |
| Reporting group description: | |
| Subjects aged between, and including, 42 and 69 days at the time of first vaccination received 3 doses of Infanrix IPV and Hiberix co-administered at separate injection sites at 2, 4 and 6 months of age, 3 dose of Synflorix at 6 weeks, 3.5 and 5.5 months of age and 2 doses of Rotarix at 6 weeks and 3.5 months of age. The Infanrix IPV was administered intramuscularly in the right thigh, the Synflorix and Hiberix vaccines were administered intramuscularly in the left thigh and the Rotarix vaccine was administered orally. | |

Primary: Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies

| | |
|---|--|
| End point title | Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies |
| End point description: | |
| A seroprotected subject was defined as a vaccinated subject who had an anti-D and anti-T antibody concentration greater to or above (\geq) 0.1 international units per milliliter (IU/mL). The Month 5 results are the primary outcome variables. | |
| End point type | Primary |
| End point timeframe: | |
| At Month 0 and Month 5 | |

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|-----------------------------|------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 217 | | |
| Units: Subjects | | | | |
| Anti-D at Month 0 | 29 | 30 | | |
| Anti-D at Month 5 | 213 | 217 | | |
| Anti-T at Month 0 | 64 | 76 | | |
| Anti-T at Month 5 | 213 | 217 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Difference in seroprotection rates for anti-D |
| Statistical analysis description: | |
| To demonstrate that the immunogenicity of the Infanrix™-IPV+Hib vaccine administered at 2, 4 and 6 months of age was non-inferior to that of the concomitant administration of the Infanrix™ IPV and Hiberix™ vaccines, in terms of immune response to all vaccine antigens, one month after the third dose | |

of the primary vaccination.

| | |
|---|---|
| Comparison groups | Infanrix IPV Group v Infanrix-IPV+Hib Group |
| Number of subjects included in analysis | 430 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | Difference in seroprotection rate |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.74 |
| upper limit | 1.78 |

Notes:

[1] - UL of the standardized asymptotic 95% CI on the group difference [Infanrix-IPV+Hib Group minus Infanrix IPV Group] in percentage of seroprotected subjects $\leq 10\%$

| | |
|-----------------------------------|---|
| Statistical analysis title | Difference in seroprotection rates for anti-T |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate that the immunogenicity of the Infanrix™-IPV+Hib vaccine administered at 2, 4 and 6 months of age was non-inferior to that of the concomitant administration of the Infanrix™ IPV and Hiberix™ vaccines, in terms of immune response to all vaccine antigens, one month after the third dose of the primary vaccination.

| | |
|---|---|
| Comparison groups | Infanrix-IPV+Hib Group v Infanrix IPV Group |
| Number of subjects included in analysis | 430 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Parameter estimate | Difference in seroprotection rate |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.74 |
| upper limit | 1.78 |

Notes:

[2] - UL of the standardized asymptotic 95% CI on the group difference [Infanrix-IPV+Hib Group minus Infanrix IPV Group] in percentage of seroprotected subjects $\leq 10\%$

Primary: Number of seroprotected subjects for anti-polyribosyl-ribitol-phosphate (anti-PRP) antibodies

| | |
|-----------------|---|
| End point title | Number of seroprotected subjects for anti-polyribosyl-ribitol-phosphate (anti-PRP) antibodies |
|-----------------|---|

End point description:

A seroprotected subject was defined as a vaccinated subject who had an anti-PRP antibody concentration ≥ 0.15 micrograms per milliliter ($\mu\text{g/mL}$). The Month 5 results are the primary outcome variables.

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

End point timeframe:

At Month 0 and Month 5

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|-----------------------------|------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 217 | | |
| Units: Subjects | | | | |
| Anti-PRP at Month 0 | 91 | 109 | | |
| Anti-PRP at Month 5 | 213 | 217 | | |

Statistical analyses

| Statistical analysis title | Difference in seroprotection rates for anti-PRP |
|--|--|
| Statistical analysis description: | |
| To demonstrate that the immunogenicity of the Infanrix™-IPV+Hib vaccine administered at 2, 4 and 6 months of age was non-inferior to that of the concomitant administration of the Infanrix™ IPV and Hiberix™ vaccines, in terms of immune response to all vaccine antigens, one month after the third dose of the primary vaccination. | |
| Comparison groups | Infanrix-IPV+Hib Group v Infanrix IPV Group |
| Number of subjects included in analysis | 430 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| Parameter estimate | Difference in seroprotection rate |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.74 |
| upper limit | 1.78 |

Notes:

[3] - UL of the standardized asymptotic 95% CI on the group difference [**Infanrix-IPV+Hib Group** minus **Infanrix IPV Group**] in percentage of seroprotected subjects ≤ 10%

Primary: Concentrations for anti-D and anti-T antibodies

| End point title | Concentrations for anti-D and anti-T antibodies ^[4] |
|---|--|
| End point description: | |
| Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was 0.1 IU/mL. | |
| End point type | Primary |
| End point timeframe: | |
| At Month 0 and Month 5 | |

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|--|------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 217 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |

| | | | | |
|-------------------|--------------------------|---------------------------|--|--|
| Anti-D at Month 0 | 0.058 (0.055 to 0.061) | 0.06 (0.056 to 0.064) | | |
| Anti-D at Month 5 | 8.096 (7.52 to 8.717) | 8.692 (8.125 to 9.298) | | |
| Anti-T at Month 0 | 0.081 (0.072 to 0.09) | 0.091 (0.08 to 0.103) | | |
| Anti-T at Month 5 | 10.259 (9.654 to 10.902) | 12.421 (11.599 to 13.301) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects seroprotected for anti-Polio virus type 1, 2 and 3 antibodies

| | |
|----------------------------------|--|
| End point title | Number of subjects seroprotected for anti-Polio virus type 1, 2 and 3 antibodies |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| At one month after (POST) Dose 3 | |

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|--------------------------------|------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 212 | 216 | | |
| Units: Subjects | | | | |
| Anti-Polio 1, POST [N=212;216] | 212 | 216 | | |
| Anti-Polio 2, POST [N=204;211] | 204 | 211 | | |
| Anti-polio 3, POST [N=198;199] | 197 | 197 | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Difference in seroprotection rates for anti-Polio1 |
| Statistical analysis description: | |
| To demonstrate that the immunogenicity of the Infanrix™-IPV+Hib vaccine administered at 2, 4 and 6 months of age was non-inferior to that of the concomitant administration of GSK Biologicals' <i>Infanrix™</i> IPV and Hiberix™ vaccines, in terms of immune response to anti-Polio type 1 antibodies, one month after the third dose of the primary vaccination. | |
| Comparison groups | Infanrix IPV Group v Infanrix-IPV+Hib Group |

| | |
|---|------------------------------------|
| Number of subjects included in analysis | 428 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[5] |
| Parameter estimate | Difference in seroprotection rates |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.75 |
| upper limit | 1.78 |

Notes:

[5] - The upper limits of the standardized asymptotic 95% confidence interval (CI) on the group differences [Infanrix IPV Group minus Infanrix-IPV+Hib Group] in percentages of subjects seroprotected against poliovirus type 1 was $\leq 10\%$.

| | |
|-----------------------------------|--|
| Statistical analysis title | Difference in seroprotection rates for anti-Polio2 |
|-----------------------------------|--|

Statistical analysis description:

To demonstrate that the immunogenicity of the Infanrix™-IPV+Hib vaccine administered at 2, 4 and 6 months of age was non-inferior to that of the concomitant administration of GSK Biologicals' Infanrix™ IPV and Hiberix™ vaccines, in terms of immune response to anti-Polio type 2 antibodies, one month after the third dose of the primary vaccination.

| | |
|---|---|
| Comparison groups | Infanrix-IPV+Hib Group v Infanrix IPV Group |
| Number of subjects included in analysis | 428 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[6] |
| Parameter estimate | Difference in seroprotection rates |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.79 |
| upper limit | 1.85 |

Notes:

[6] - The upper limits of the standardized asymptotic 95% confidence interval (CI) on the group differences [Infanrix IPV Group minus Infanrix-IPV+Hib Group] in percentages of subjects seroprotected against poliovirus type 2 was $\leq 10\%$.

| | |
|-----------------------------------|--|
| Statistical analysis title | Difference in seroprotection rates for anti-Polio3 |
|-----------------------------------|--|

Statistical analysis description:

To demonstrate that the immunogenicity of the Infanrix™-IPV+Hib vaccine administered at 2, 4 and 6 months of age was non-inferior to that of the concomitant administration of GSK Biologicals' Infanrix™ IPV and Hiberix™ vaccines, in terms of immune response to anti-Polio type 3 antibodies, one month after the third dose of the primary vaccination.

| | |
|---|---|
| Comparison groups | Infanrix IPV Group v Infanrix-IPV+Hib Group |
| Number of subjects included in analysis | 428 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[7] |
| Parameter estimate | Difference in seroprotection rates |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.14 |
| upper limit | 1.89 |

Notes:

[7] - The upper limits of the standardized asymptotic 95% confidence interval (CI) on the group differences [Infanrix IPV Group minus Infanrix-IPV+Hib Group] in percentages of subjects seroprotected against poliovirus type 3 was $\leq 10\%$.

Primary: Anti-pertussis toxoid (PT), anti-filamentous haemagglutinin (FHA) and anti-pertactin (PRN) antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-pertussis toxoid (PT), anti-filamentous haemagglutinin (FHA) and anti-pertactin (PRN) antibody concentrations |
|-----------------|--|

End point description:

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

End point timeframe:

At one month after (POST) Dose 3

| End point values | Infanrix- IPV+Hib Group | Infanrix IPV Group | | |
|--|----------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 217 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT [N=213;217] | 54.2 (50.4 to 58.3) | 56 (51.8 to 60.5) | | |
| Anti-FHA [N=213;217] | 125 (115.4 to 135.4) | 134.2 (124.2 to 145) | | |
| Anti-PRN [N=213;217] | 125.8 (116 to 136.5) | 133.4 (123 to 144.6) | | |

Statistical analyses

| | |
|----------------------------|-------------------------------------|
| Statistical analysis title | Difference in GMC ratio for anti-PT |
|----------------------------|-------------------------------------|

Statistical analysis description:

To demonstrate that the immunogenicity of the Infanrix™-IPV+Hib vaccine administered at 2, 4 and 6 months of age was non-inferior to that of the concomitant administration of GSK Biologicals' Infanrix™ IPV and Hiberix™ vaccines, in terms of immune response to anti-PT antigens, one month after the third dose of the primary vaccination.

| | |
|---|---|
| Comparison groups | Infanrix IPV Group v Infanrix-IPV+Hib Group |
| Number of subjects included in analysis | 430 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[8] |
| Method | ANCOVA |
| Parameter estimate | Difference in GMC ratio |
| Point estimate | 1.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.93 |
| upper limit | 1.15 |

Notes:

[8] - The upper limits of the 95% confidence interval (CI) on the group ratio [Infanrix IPV Group divided by Infanrix-IPV+Hib Group] of geometric mean concentrations (GMCs) of antibodies against pertussis toxoid (PT) was ≤ 1.5 .

| | |
|-----------------------------------|--------------------------------------|
| Statistical analysis title | Difference in GMC ratio for anti-FHA |
|-----------------------------------|--------------------------------------|

Statistical analysis description:

To demonstrate that the immunogenicity of the Infanrix™-IPV+Hib vaccine administered at 2, 4 and 6 months of age was non-inferior to that of the concomitant administration of GSK Biologicals' Infanrix™ IPV and Hiberix™ vaccines, in terms of immune response to anti-FHA antigens, one month after the third dose of the primary vaccination.

| | |
|---|---|
| Comparison groups | Infanrix-IPV+Hib Group v Infanrix IPV Group |
| Number of subjects included in analysis | 430 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[9] |
| Method | ANCOVA |
| Parameter estimate | Difference in GMC ratio |
| Point estimate | 1.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.97 |
| upper limit | 1.21 |

Notes:

[9] - The upper limits of the 95% confidence interval (CI) on the group ratio [Infanrix IPV Group divided by Infanrix-IPV+Hib Group] of geometric mean concentrations (GMCs) of antibodies against filamentous haemagglutinin (FHA) was ≤ 1.5 .

| | |
|-----------------------------------|--------------------------------------|
| Statistical analysis title | Difference in GMC ratio for anti-PRN |
|-----------------------------------|--------------------------------------|

Statistical analysis description:

To demonstrate that the immunogenicity of the Infanrix™-IPV+Hib vaccine administered at 2, 4 and 6 months of age was non-inferior to that of the concomitant administration of GSK Biologicals' Infanrix™ IPV and Hiberix™ vaccines, in terms of immune response to anti-PRN antigens, one month after the third dose of the primary vaccination.

| | |
|---|---|
| Comparison groups | Infanrix-IPV+Hib Group v Infanrix IPV Group |
| Number of subjects included in analysis | 430 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[10] |
| Method | ANCOVA |
| Parameter estimate | Difference in GMC ratio |
| Point estimate | 1.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.96 |
| upper limit | 1.21 |

Notes:

[10] - The upper limits of the 95% confidence interval (CI) on the group ratio [Infanrix IPV Group divided by Infanrix-IPV+Hib Group] of geometric mean concentrations (GMCs) of antibodies against pertactin (PRN) was ≤ 1.5 .

Primary: Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentrations equal to or above (\geq) the cut-off value of 5 ELISA units per millilitre (EL.U/mL)

| | |
|-----------------|---|
| End point title | Number of subjects with anti-PT, anti-FHA and anti-PRN antibody concentrations equal to or above (\geq) the cut-off value of 5 ELISA units per millilitre (EL.U/mL) ^[11] |
|-----------------|---|

End point description:

Results for the one month after (POST) Dose 3 vaccination timepoint were the primary outcome.

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

End point timeframe:

Prior to vaccination (PRE) and one month after (POST) Dose 3

Notes:

[11] - 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

| End point values | Infanrix- IPV+Hib Group | Infanrix IPV Group | | |
|-----------------------------|----------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 217 | | |
| Units: Subjects | | | | |
| Anti-PT, PRE [N=212;216] | 27 | 34 | | |
| Anti-PT, POST [N=213;217] | 213 | 217 | | |
| Anti-FHA, PRE [N=211;214] | 170 | 178 | | |
| Anti-FHA, POST [N=213;217] | 213 | 217 | | |
| Anti-PRN, PRE [N=213;217] | 25 | 30 | | |
| Anti-PRN, POST [N=213;217] | 213 | 217 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms

| | |
|-----------------|--|
| End point title | Number of subjects with any solicited local symptoms |
|-----------------|--|

End point description:

Assessed solicited local symptoms were pain, redness and swelling at the injection site. Any = incidence of a particular symptom regardless of intensity grade.

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

End point timeframe:

During the 4-day (Days 0-3) follow-up period after any vaccination with Infanrix™-IPV+Hib or Infanrix™ IPV + Hiberix™

| End point values | Infanrix- IPV+Hib Group | Infanrix IPV Group | | |
|-----------------------------|----------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 224 | 227 | | |
| Units: Subjects | | | | |
| Any Pain | 143 | 146 | | |
| Any Redness | 177 | 167 | | |
| Any Swelling | 130 | 121 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms

| | |
|-----------------|--|
| End point title | Number of subjects with any solicited general symptoms |
|-----------------|--|

End point description:

Assessed solicited general symptoms were drowsiness, irritability/fussiness, loss of appetite and fever [defined as tympanic temperature ≥ 37.5 degrees Celsius ($^{\circ}\text{C}$)]. Any = incidence of a particular symptom regardless of intensity grade.

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

End point timeframe:

During the 4-day (Days 0-3) follow-up period after any vaccination with InfanrixTM-IPV+Hib or InfanrixTM IPV + HiberixTM

| End point values | Infanrix- IPV+Hib Group | Infanrix IPV Group | | |
|---|----------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 224 | 227 | | |
| Units: Subjects | | | | |
| Any Drowsiness | 153 | 147 | | |
| Any Irritability/Fussiness | 181 | 182 | | |
| Any Loss of appetite | 120 | 103 | | |
| Temperature $\geq 37.5^{\circ}\text{C}$ | 83 | 81 | | |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any = any unsolicited AE regardless of intensity or relationship to vaccination.

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

End point timeframe:

During the 31-day (Days 0-30) follow-up period after any vaccination with InfanrixTM-IPV+Hib or InfanrixTM IPV + HiberixTM

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|-----------------------------|------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 224 | 227 | | |
| Units: Subjects | | | | |
| Any AEs | 130 | 123 | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|---|---|
| End point title | Number of subjects with any serious adverse events (SAEs) |
| End point description: Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. | |
| End point type | Secondary |
| End point timeframe: During the entire study period (from Month 0 to Month 5 ½) | |

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|-----------------------------|------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 224 | 227 | | |
| Units: Subjects | | | | |
| Any SAEs | 25 | 21 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of anti-PRN antibodies

| | |
|---|---------------------------------------|
| End point title | Concentrations of anti-PRN antibodies |
| End point description: Concentrations were expressed as geometric mean concentrations (GMCs). The seropositivity cut-off of the assay was 5 EL.U/mL. | |
| End point type | Secondary |
| End point timeframe: At Month 0 and Month 5 | |

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|--|------------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 217 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRN at Month 0 | 2.9 (2.7 to 3) | 3.1 (2.8 to 3.3) | | |
| Anti-PRN at Month 5 | 125.8 (116 to 136.5) | 133.4 (123 to 144.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of anti-PRP antibodies

| | |
|--|---------------------------------------|
| End point title | Concentrations of anti-PRP antibodies |
| End point description: Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was 0.15 µg/mL. | |
| End point type | Secondary |
| End point timeframe: At Month 0 and Month 5 | |

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|--|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 217 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP at Month 0 | 0.165 (0.143 to 0.191) | 0.219 (0.184 to 0.26) | | |
| Anti-PRP at Month 5 | 8.456 (7.283 to 9.819) | 18.7 (16.353 to 21.384) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a vaccine response

| | |
|--|--|
| End point title | Number of subjects with a vaccine response |
| End point description: Vaccine response was defined as antibody concentration \geq 5 EL.U/mL at post vaccination, for initially seronegative subjects, and at least maintenance of antibody concentration from pre to post-vaccination (i.e. antibody concentration at post vaccination \geq 1 fold the pre-vaccination antibody concentration), for initially seropositive subjects. | |

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Month 5 | |

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|-----------------------------|------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 217 | | |
| Units: Subjects | 213 | 216 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-Polio type 1, 2 and 3

| | |
|------------------------|---|
| End point title | Number of seroprotected subjects for anti-Polio type 1, 2 and 3 |
| End point description: | |

| | |
|----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Prior to vaccination (PRE) | |

| End point values | Infanrix-IPV+Hib Group | Infanrix IPV Group | | |
|-------------------------------|------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 211 | 216 | | |
| Units: Subjects | | | | |
| Anti-Polio 1, PRE [N=211;216] | 104 | 89 | | |
| Anti-Polio 2, PRE [N=211;214] | 119 | 108 | | |
| Anti-Polio 3, PRE [N=211;216] | 41 | 31 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Polio type 1, 2 and 3 antibody titers

| | |
|------------------------|--|
| End point title | Anti-Polio type 1, 2 and 3 antibody titers |
| End point description: | |

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Prior to vaccination (PRE) and one month after (POST) Dose 3 | |

| End point values | Infanrix- IPV+Hib Group | Infanrix IPV Group | | |
|--|----------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 212 | 216 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Polio 1, PRE [N=211;216] | 9.5 (8.3 to 11) | 9.4 (8 to 11) | | |
| Anti-Polio 1, POST [N=212;216] | 328.8 (289.8 to 373.1) | 372.7 (323.8 to 428.9) | | |
| Anti-Polio 2, PRE [N=211;214] | 10.8 (9.4 to 12.5) | 8.8 (7.7 to 9.9) | | |
| Anti-Polio 2 POST [N=204;211] | 340.6 (295.4 to 392.6) | 400.2 (347.6 to 460.7) | | |
| Anti-Polio 3, PRE [N=211;216] | 5.5 (5 to 6.1) | 4.9 (4.5 to 5.3) | | |
| Anti-Polio 3, POST [N=198;199] | 377.7 (322.3 to 442.6) | 465.3 (390.3 to 554.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

| | |
|----------------------------|--|
| End point title | Anti-PT, anti-FHA and anti-PRN antibody concentrations |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Prior to vaccination (PRE) | |

| End point values | Infanrix- IPV+Hib Group | Infanrix IPV Group | | |
|--|----------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 217 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT, PRE [N=212;216] | 3 (2.8 to 3.2) | 3.1 (2.9 to 3.3) | | |
| Anti-FHA, PRE [N=211;214] | 10.5 (9.3 to 12) | 11.7 (10.3 to 13.3) | | |
| Anti-PRN, PRE [N=213;217] | 2.9 (2.7 to 3) | 3.1 (2.8 to 3.3) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAE(s): during the entire study period (Month 0 to Month 5 ½); Solicited local/general symptoms: during the 4-day (Days 0-3) follow-up period after any vaccination; Unsolicited AE(s): during the 31-day (Days 0-30) follow-up period after any vaccination.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Infanrix IPV Group |
|-----------------------|--------------------|

Reporting group description:

Subjects aged between, and including, 42 and 69 days at the time of first vaccination received 3 doses of Infanrix IPV and Hiberix co-administered at separate injection sites at 2, 4 and 6 months of age, 3 dose of Synflorix at 6 weeks, 3.5 and 5.5 months of age and 2 doses of Rotarix at 6 weeks and 3.5 months of age. The Infanrix IPV was administered intramuscularly in the right thigh, the Synflorix and Hiberix vaccines were administered intramuscularly in the left thigh and the Rotarix vaccine was administered orally.

| | |
|-----------------------|------------------------|
| Reporting group title | Infanrix-IPV+Hib Group |
|-----------------------|------------------------|

Reporting group description:

Subjects aged between, and including, 42 and 69 days at the time of first vaccination received 3 doses of Infanrix-IPV+Hib at 2, 4 and 6 months of age, 3 doses of Synflorix at 6 weeks, 3.5 and 5.5 months of age and 2 doses of Rotarix at 6 weeks and 3.5 months of age. The Infanrix-IPV+Hib was administered intramuscularly in the right thigh, the Synflorix vaccine was administered intramuscularly in the left thigh and the Rotarix vaccine was administered orally.

| Serious adverse events | Infanrix IPV Group | Infanrix-IPV+Hib Group | |
|---|--------------------|------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 21 / 227 (9.25%) | 25 / 224 (11.16%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Skull fracture | | | |
| subjects affected / exposed | 1 / 227 (0.44%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 227 (0.44%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 227 (0.00%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 227 (0.44%) | 0 / 224 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intussusception | | | |
| subjects affected / exposed | 0 / 227 (0.00%) | 1 / 224 (0.45%) | |
| 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 | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 227 (0.44%) | 0 / 224 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Vesicoureteric reflux | | | |
| subjects affected / exposed | 1 / 227 (0.44%) | 0 / 224 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 5 / 227 (2.20%) | 7 / 224 (3.13%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 6 / 227 (2.64%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 227 (0.44%) | 5 / 224 (2.23%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 227 (0.44%) | 4 / 224 (1.79%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 3 / 227 (1.32%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 227 (0.00%) | 2 / 224 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 227 (0.00%) | 2 / 224 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 227 (0.00%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 0 / 227 (0.00%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis | | | |
| subjects affected / exposed | 0 / 227 (0.00%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 227 (0.00%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis chronic | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 227 (0.44%) | 0 / 224 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchitis | | | |
| subjects affected / exposed | 0 / 227 (0.00%) | 1 / 224 (0.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 227 (0.44%) | 0 / 224 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Infanrix IPV Group | Infanrix-IPV+Hib Group | |
|---|--------------------|------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 220 / 227 (96.92%) | 218 / 224 (97.32%) | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 146 / 227 (64.32%) | 143 / 224 (63.84%) | |
| occurrences (all) | 146 | 143 | |
| Redness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 167 / 227 (73.57%) | 177 / 224 (79.02%) | |
| occurrences (all) | 167 | 177 | |
| Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 121 / 227 (53.30%) | 130 / 224 (58.04%) | |
| occurrences (all) | 121 | 130 | |
| Drowsiness | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|--------------------|--------------------|--|
| subjects affected / exposed | 147 / 227 (64.76%) | 153 / 224 (68.30%) | |
| occurrences (all) | 147 | 153 | |
| Irritability/Fussiness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 182 / 227 (80.18%) | 181 / 224 (80.80%) | |
| occurrences (all) | 182 | 181 | |
| Loss of appetite | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 103 / 227 (45.37%) | 120 / 224 (53.57%) | |
| occurrences (all) | 103 | 120 | |
| Temperature (Tympanic) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 81 / 227 (35.68%) | 83 / 224 (37.05%) | |
| occurrences (all) | 81 | 83 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 227 (4.41%) | 29 / 224 (12.95%) | |
| occurrences (all) | 10 | 29 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 29 / 227 (12.78%) | 37 / 224 (16.52%) | |
| occurrences (all) | 29 | 37 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 29 / 227 (12.78%) | 34 / 224 (15.18%) | |
| occurrences (all) | 29 | 34 | |
| Bronchitis | | | |
| subjects affected / exposed | 14 / 227 (6.17%) | 14 / 224 (6.25%) | |
| occurrences (all) | 14 | 14 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 13 / 227 (5.73%) | 14 / 224 (6.25%) | |
| occurrences (all) | 13 | 14 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported