



Clinical trial results:

A phase IV, non-randomised, open-label, multicentre study with two parallel groups to assess the immunogenicity and safety of GlaxoSmithKline (GSK) Biologicals' combined DTPa-HBV-IPV/Hib vaccine administered as a three-dose primary vaccination course at 2, 4 and 6 months of age in healthy infants in Canada.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-003428-34 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 12 March 2013 |

Results information

| | |
|--------------------------------|-------------|
| Result version number | v1 |
| This version publication date | 11 May 2016 |
| First version publication date | 30 May 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 103506 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00753649 |
| 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, 044 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 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 | 28 November 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 12 March 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 March 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the immune response to the Hib component of GSK Biologicals' combined DTPa-HBV-IPV/Hib preservative-free vaccine in terms of seroprotection rates one month after the three-dose primary vaccination course in "Aboriginal infants" and "Other Non-Aboriginal infants".

Protection of trial subjects:

All subjects were supervised after vaccination/product administration 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.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 23 September 2008 |
| 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 | Canada: 224 |
| Worldwide total number of subjects | 224 |
| 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) | 224 |
| 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 Study (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 Hexa Aboriginal Group |

Arm description: -

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Infanrix™ Hexa |
| Investigational medicinal product code | |
| Other name | DTPa-HBV-IPV/Hib |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Three doses of **Infanrix Hexa™** vaccine were administered by injection, intramuscularly in the right side of the thigh, at 2, 4 and 6 months of age.

| | |
|--|------------|
| Investigational medicinal product name | Rotarix™ |
| Investigational medicinal product code | |
| Other name | HRV |
| Pharmaceutical forms | Oral drops |
| Routes of administration | Oral use |

Dosage and administration details:

Two doses of **Rotarix™** vaccine were administered concomitantly with the first two doses of **Infanrix Hexa™** vaccine. **Rotarix™** was given orally at 2 and 4 months of age, according to the immunization schedule.

| | |
|------------------|------------------------------------|
| Arm title | Infanrix Hexa Non-Aboriginal Group |
|------------------|------------------------------------|

Arm description: -

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Infanrix™ Hexa |
| Investigational medicinal product code | |
| Other name | DTPa-HBV-IPV/Hib |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Three doses of **Infanrix Hexa™** vaccine were administered by injection, intramuscularly in the right side of the thigh, at 2, 4 and 6 months of age.

| | |
|--|------------|
| Investigational medicinal product name | Rotarix™ |
| Investigational medicinal product code | |
| Other name | HRV |
| Pharmaceutical forms | Oral drops |

| | |
|--------------------------|----------|
| Routes of administration | Oral use |
|--------------------------|----------|

Dosage and administration details:

Two doses of Rotarix™ vaccine were administered concomitantly with the first two doses of Infanrix Hexa™ vaccine. Rotarix™ was given orally at 2 and 4 months of age, according to the immunization schedule.

| Number of subjects in period 1 | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non- Aboriginal Group |
|---|-----------------------------------|--|
| Started | 112 | 112 |
| Completed | 105 | 112 |
| Not completed | 7 | 0 |
| Lost to follow-up (subjects with complete vaccinat | 1 | - |
| Protocol Violation | 2 | - |
| Lost to follow-up (subjects with incomplete vaccin | 3 | - |
| Migrated/moved from study area | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Infanrix Hexa Aboriginal Group |
|-----------------------|--------------------------------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| | |
|-----------------------|------------------------------------|
| Reporting group title | Infanrix Hexa Non-Aboriginal Group |
|-----------------------|------------------------------------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| Reporting group values | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | Total |
|--|--------------------------------|------------------------------------|-------|
| Number of subjects | 112 | 112 | 224 |
| 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 | 9.3 | 9.2 | |
| standard deviation | ± 1.38 | ± 1.3 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 62 | 52 | 114 |
| Male | 50 | 60 | 110 |

End points

End points reporting groups

| | |
|--------------------------------|------------------------------------|
| Reporting group title | Infanrix Hexa Aboriginal Group |
| Reporting group description: - | |
| Reporting group title | Infanrix Hexa Non-Aboriginal Group |
| Reporting group description: - | |

Primary: Number of seroprotected subjects against Polyribosyl-ribitol phosphate (anti-PRP)

| | |
|------------------------|--|
| End point title | Number of seroprotected subjects against Polyribosyl-ribitol phosphate (anti-PRP) ^[1] |
| End point description: | A seroprotected subject was a subject whose anti-PRP antibody concentration was ≥ 0.15 $\mu\text{g/mL}$. |
| End point type | Primary |
| End point timeframe: | One month after (POST) Dose 3. |

Notes:

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

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

| End point values | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | | |
|------------------------------|--------------------------------|------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 94 | 107 | | |
| Units: Subjects | | | | |
| Anti-PRP, POST-M1 [N=94,107] | 92 | 106 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-Polyribosyl-ribitol phosphate (anti-PRP) antibodies with concentrations $\geq 1\mu\text{g/mL}$

| | |
|------------------------|---|
| End point title | Number of subjects with anti-Polyribosyl-ribitol phosphate (anti-PRP) antibodies with concentrations $\geq 1\mu\text{g/mL}$ |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | One month after (POST) Dose 3. |

| End point values | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | | |
|------------------------------|--------------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 94 | 107 | | |
| Units: Subjects | | | | |
| Anti-PRP, POST-M1 [N=94,107] | 83 | 91 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

| | |
|--------------------------------|----------------------------------|
| End point title | Anti-PRP antibody concentrations |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| One month after (POST) Dose 3. | |

| End point values | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | | |
|--|--------------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 94 | 107 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP, POST-M1 [N=94,107] | 6.123 (4.498 to 8.334) | 3.51 (2.745 to 4.488) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against Hepatitis B (anti-HBs), with anti-HBs antibody concentrations ≥ 10 µg/mL

| | |
|--------------------------------|---|
| End point title | Number of seroprotected subjects against Hepatitis B (anti-HBs), with anti-HBs antibody concentrations ≥ 10 µg/mL |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| One month after (POST) Dose 3. | |

| End point values | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | | |
|------------------------------|--------------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 103 | | |
| Units: Subjects | | | | |
| Anti-HBs, POST-M1 [N=91,103] | 91 | 103 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-HBs antibody concentrations ≥ 100 mIU/mL

| | |
|--------------------------------|--|
| End point title | Number of subjects with Anti-HBs antibody concentrations ≥ 100 mIU/mL |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| One month after (POST) Dose 3. | |

| End point values | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | | |
|------------------------------|--------------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 103 | | |
| Units: Subjects | | | | |
| Anti-HBs, POST-M1 [N=91,103] | 89 | 100 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

| | |
|--------------------------------|----------------------------------|
| End point title | Anti-HBs antibody concentrations |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| One month after (POST) Dose 3. | |

| End point values | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | | |
|---|--------------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 103 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HBs, POST-M1 [N=91,103] | 1797.9 (1375.1 to 2350.7) | 1544.4 (1210.4 to 1970.5) | | |

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: | |
| End point type | Secondary |
| End point timeframe: | |
| During the 31 day (Days 0-30) post vaccination | |

| End point values | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | | |
|-----------------------------|--------------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 112 | 112 | | |
| Units: Subjects | | | | |
| Any AEs, [N=112,112] | 26 | 19 | | |

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: | |
| End point type | Secondary |

End point timeframe:

During the entire study period

| End point values | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | | |
|-----------------------------|--------------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 112 | 112 | | |
| Units: Subjects | | | | |
| Any SAEs, [N=112.112] | 6 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited AEs during the 31-day post-vaccination period, SAEs during the entire period

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Infanrix Hexa Aboriginal Group |
|-----------------------|--------------------------------|

Reporting group description: -

| | |
|-----------------------|------------------------------------|
| Reporting group title | Infanrix Hexa Non-Aboriginal Group |
|-----------------------|------------------------------------|

Reporting group description: -

| Serious adverse events | Infanrix Hexa Aboriginal Group | Infanrix Hexa Non-Aboriginal Group | |
|--|--------------------------------|------------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 112 (5.36%) | 0 / 112 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | 0 / 112 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile convulsion | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 112 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 112 (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 | 1 / 112 (0.89%) | 0 / 112 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 112 (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 infection | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 112 (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 Hexa Aboriginal Group | Infanrix Hexa Non- Aboriginal Group | |
|---|-----------------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 26 / 112 (23.21%) | 19 / 112 (16.96%) | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 26 / 112 (23.21%) | 19 / 112 (16.96%) | |
| occurrences (all) | 26 | 19 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 24 June 2010 | <p>Amendment 2</p> <p>The protocol was originally designed for sites in British Columbia (BC) and therefore the vaccines that the subject may receive outside of the study were recommended according to the BC vaccination schedule. New sites were selected in provinces where the recommended schedule for vaccine co-administration is different from BC, therefore the protocol is being amended to allow vaccine coadministration according to the provincial schedule rather than the BC schedules.</p> <ul style="list-style-type: none">• Some formatting errors have been corrected in the protocol. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported