



Clinical trial results:

An open, phase IV, non-randomised, single-centre study with two study groups to assess the immunogenicity and reactogenicity of a booster dose of GlaxoSmithKline (GSK) Biologicals' combined reduced antigen content diphtheria-tetanus toxoids and acellular pertussis vaccine (Boostrix), when administered in young adults, 10 years after previous booster vaccination in study 263855/004 (dTpa-004).

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2007-003248-31 |
| Trial protocol | FI |
| Global end of trial date | 30 April 2008 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 10 March 2016 |
| First version publication date | 06 June 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 110806 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00610168 |
| 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 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 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? | No |

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 01 October 2008 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 April 2008 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 April 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that a booster dose of dTpa vaccine, administered to young adults 10 years after a previous dose of the dTpa vaccine, elicited seroprotective antibody concentrations in at least 80% of the subjects against diphtheria and in at least 90% of the subjects against tetanus one month after the booster dose.

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 January 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 | Finland: 82 |
| Worldwide total number of subjects | 82 |
| EEA total number of subjects | 82 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 82 |
| 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 (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Boostrix I Group |

Arm description:

Subjects who had received the dTpa vaccine in the primary study (263855/004)

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Boostrix™ |
| Investigational medicinal product code | |
| Other name | dTPa vaccine |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single booster dose of dTpa vaccine administered intramuscularly in the deltoid region of the non-dominant arm.

| | |
|------------------|-------------------|
| Arm title | Boostrix II Group |
|------------------|-------------------|

Arm description:

Subjects who had received the Td + pa vaccines in the primary study (263855/004)

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Boostrix™ |
| Investigational medicinal product code | |
| Other name | dTPa vaccine |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single booster dose of dTpa vaccine administered intramuscularly in the deltoid region of the non-dominant arm.

| Number of subjects in period 1 | Boostrix I Group | Boostrix II Group |
|--------------------------------|------------------|-------------------|
| Started | 75 | 7 |
| Completed | 73 | 7 |
| Not completed | 2 | 0 |
| Consent withdrawn by subject | 2 | - |

Baseline characteristics

Reporting groups

| | |
|--|-------------------|
| Reporting group title | Boostrix I Group |
| Reporting group description: | |
| Subjects who had received the dTpa vaccine in the primary study (263855/004) | |
| Reporting group title | Boostrix II Group |
| Reporting group description: | |
| Subjects who had received the Td + pa vaccines in the primary study (263855/004) | |

| Reporting group values | Boostrix I Group | Boostrix II Group | Total |
|---|------------------|-------------------|-------|
| Number of subjects | 75 | 7 | 82 |
| 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: years | | | |
| arithmetic mean | 21.1 | 21.1 | |
| standard deviation | ± 0.31 | ± 0.38 | - |
| Gender categorical Units: Subjects | | | |
| Female | 66 | 6 | 72 |
| Male | 9 | 1 | 10 |

End points

End points reporting groups

| | |
|---|-----------------------|
| Reporting group title | Boostrix I Group |
| Reporting group description: Subjects who had received the dTpa vaccine in the primary study (263855/004) | |
| Reporting group title | Boostrix II Group |
| Reporting group description: Subjects who had received the Td + pa vaccines in the primary study (263855/004) | |
| Subject analysis set title | Boostrix Pooled Group |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: For safety assessment, the 2 groups (Boostrix I Group + Boostrix II Group) were pooled (Pooled Group). | |

Primary: Number of subjects with anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations equal to or above (\geq) 0.1 international units per milliliter (IU/mL) and ≥ 1 IU/mL

| | |
|--|--|
| End point title | Number of subjects with anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations equal to or above (\geq) 0.1 international units per milliliter (IU/mL) and ≥ 1 IU/mL ^[1] |
| End point description: The primary efficacy results were reported for the Boostrix I Group one month after the booster dose | |
| End point type | Primary |
| End point timeframe: Prior to and one month after the booster vaccination in all subjects | |

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 | Boostrix I Group | Boostrix II Group | | |
|--|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 74 | 7 | | |
| Units: Subjects | | | | |
| Anti-diphtheria ≥ 0.1 IU/mL Pre [N=74;7] | 61 | 5 | | |
| Anti-diphtheria ≥ 0.1 IU/mL Post [N=73;7] | 73 | 7 | | |
| Anti-diphtheria ≥ 1 IU/mL Pre [N=74;7] | 17 | 0 | | |
| Anti-diphtheria ≥ 1 IU/mL Post [N=73;7] | 68 | 7 | | |
| Anti-tetanus ≥ 0.1 IU/mL Pre [N=74;7] | 72 | 7 | | |
| Anti-tetanus ≥ 0.1 IU/mL Post [N=73;7] | 73 | 7 | | |
| Anti-tetanus ≥ 1 IU/mL Pre [N=74;7] | 44 | 4 | | |
| Anti-tetanus ≥ 1 IU/mL Post [N=73;7] | 71 | 7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-diphtheria (Anti-DT) and anti-tetanus toxoids (Anti-TT) antibody concentrations |
|-----------------|--|

End point description:

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

End point timeframe:

Prior to and one month after the booster vaccination

| End point values | Boostrix I Group | Boostrix II Group | | |
|--|-------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 74 | 7 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-diphtheria Pre [N=74;7] | 0.318 (0.24 to 0.421) | 0.196 (0.068 to 0.568) | | |
| Anti-diphtheria Post [N=73;7] | 5.994 (4.679 to 7.68) | 3.226 (1.741 to 5.975) | | |
| Anti-tetanus Pre [N=74;7] | 1.246 (0.956 to 1.623) | 0.989 (0.498 to 1.961) | | |
| Anti-tetanus Post [N=73;7] | 9.596 (7.986 to 11.531) | 8.975 (5.277 to 15.264) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations \geq 5 ELISA unit per milli-liter (EL.U/ml)

| | |
|-----------------|---|
| End point title | Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations \geq 5 ELISA unit per milli-liter (EL.U/ml) |
|-----------------|---|

End point description:

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

End point timeframe:

Prior to and one month after the booster vaccination

| End point values | Boostrix I Group | Boostrix II Group | | |
|-----------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 7 | | |
| Units: Subjects | | | | |
| Anti-PT Pre [N=75;7] | 46 | 7 | | |
| Anti-PT Post [N=73;7] | 73 | 7 | | |
| Anti-FHA Pre [N=75;7] | 75 | 7 | | |
| Anti-FHA Post [N=73;7] | 73 | 7 | | |
| Anti-PRN Pre [N=75;7] | 72 | 7 | | |
| Anti-PRN Post [N=73;7] | 73 | 7 | | |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point timeframe:

Prior to and one month after the booster vaccination

| End point values | Boostrix I Group | Boostrix II Group | | |
|--|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 7 | | |
| Units: EL.U/ml | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT Pre [N=75;7] | 9.1 (6.9 to 11.9) | 12.5 (8.8 to 17.9) | | |
| Anti-PT Post [N=73;7] | 90.3 (73.9 to 110.5) | 116.5 (56.5 to 240.5) | | |
| Anti-FHA Pre [N=75;7] | 63.8 (53.1 to 76.8) | 118.8 (80.6 to 175.1) | | |
| Anti-FHA Post [N=73;7] | 793.4 (670.3 to 939.2) | 584.3 (248.3 to 1374.9) | | |
| Anti-PRN Pre [N=75;7] | 36.9 (27.7 to 49.2) | 41.8 (20.3 to 85.9) | | |
| Anti-PRN Post [N=73;7] | 548.1 (456.9 to 657.5) | 685.3 (243.5 to 1928.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with vaccine response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

| | |
|-----------------|---|
| End point title | Number of subjects with vaccine response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) |
|-----------------|---|

End point description:

Booster response was defined as appearance of antibodies in subjects who were seronegative at the pre-vaccination time point (i.e. with concentrations < 5 IU/mL) or at least 2-fold increase of prevaccination antibody concentrations in subjects who were seropositive at the pre-vaccination time point (i.e. with concentrations ≥5 IU/mL).

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

End point timeframe:

One month after booster vaccination

| End point values | Boostrix I Group | Boostrix II Group | | |
|-----------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 7 | | |
| Units: Subjects | | | | |
| Anti-PT [N=73;7] | 72 | 7 | | |
| Anti-FHA [N=73;7] | 71 | 6 | | |
| Anti-PRN [N=73;7] | 68 | 7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and any Grade 3 solicited local symptoms

| | |
|-----------------|--|
| End point title | Number of subjects with any and any Grade 3 solicited local symptoms |
|-----------------|--|

End point description:

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

End point timeframe:

During the 4-day (Day 0–3) follow-up period after booster vaccination.

| End point values | Boostrix Pooled Group | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 81 | | | |
| Units: Subjects | | | | |
| Any pain | 76 | | | |
| Grade 3 pain | 8 | | | |
| Any redness | 48 | | | |
| Grade 3 redness | 14 | | | |
| Any swelling | 46 | | | |
| Grade 3 swelling | 15 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, any Grade 3 and related solicited general symptoms

| | |
|-----------------|---|
| End point title | Number of subjects with any, any Grade 3 and related solicited general symptoms |
|-----------------|---|

End point description:

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

End point timeframe:

During the 4-day (Day 0–3) follow-up period after booster vaccination.

| End point values | Boostrix Pooled Group | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 81 | | | |
| Units: Subjects | | | | |
| Any Fatigue | 44 | | | |
| Grade 3 Fatigue | 2 | | | |
| Related Fatigue | 36 | | | |
| Any Fever | 7 | | | |
| Grade 3 Fever | 0 | | | |
| Related Fever | 7 | | | |
| Any Gastrointestinal | 14 | | | |
| Grade 3 Gastrointestinal | 1 | | | |
| Related Gastrointestinal | 8 | | | |
| Any Headache | 27 | | | |
| Grade 3 Headache | 0 | | | |
| Related Headache | 22 | | | |

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:

For safety assessment Boostrix I Group and Boostrix II Group were pooled (Pooled Group)

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

End point timeframe:

During the 31-day (Day 0–30) follow-up period after booster vaccination

| End point values | Boostrix Pooled Group | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 82 | | | |
| Units: Subjects | | | | |
| AEs | 26 | | | |

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:

For safety assessment Boostrix I Group and Boostrix II Group were pooled (Pooled Group)

| End point values | Boostrix Pooled Group | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 82 | | | |
| Units: Subjects | | | | |
| SAEs | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 11.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Pooled Group |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events | Pooled Group | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 82 (1.22%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hyperventilation | | | |
| subjects affected / exposed | 1 / 82 (1.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Pooled Group | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 76 / 82 (92.68%) | | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[1] | 76 / 81 (93.83%) | | |
| occurrences (all) | 76 | | |
| Redness | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed ^[2] | 48 / 81 (59.26%) | | |
| occurrences (all) | 48 | | |
| Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[3] | 46 / 81 (56.79%) | | |
| occurrences (all) | 46 | | |
| Fatigue | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[4] | 44 / 81 (54.32%) | | |
| occurrences (all) | 44 | | |
| Fever (Axillary) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[5] | 7 / 81 (8.64%) | | |
| occurrences (all) | 7 | | |
| Gastrointestinal | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[6] | 14 / 81 (17.28%) | | |
| occurrences (all) | 14 | | |
| Headache | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[7] | 27 / 81 (33.33%) | | |
| occurrences (all) | 27 | | |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 6 / 82 (7.32%) | | |
| occurrences (all) | 6 | | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Solicited local and general symptoms were only reported for subjects with a symptom sheet completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Solicited local and general symptoms were only reported for subjects with a symptom sheet completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Solicited local and general symptoms were only reported for subjects with a symptom sheet completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed for the reporting group. These numbers are expected to be equal.

Justification: Solicited local and general symptoms were only reported for subjects with a symptom sheet completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Solicited local and general symptoms were only reported for subjects with a symptom sheet completed.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Solicited local and general symptoms were only reported for subjects with a symptom sheet completed.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Solicited local and general symptoms were only reported for subjects with a symptom sheet completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 22 November 2007 | <p>Amendment 1</p> <p>The immunity to pertussis induced by vaccination is known to wane over time. The necessity to maintain a sufficient immunity to pertussis disease throughout adulthood via regular boosters is being considered. One practical way to achieve this would be to use the opportunity of the currently generally recommended dT decennial booster to add on a pertussis booster, using the dTpa vaccine. The persistence of the immune response in adolescents and adults has been studied up to five years after dTpa booster vaccination. Data currently suggest that sufficient immunity is still present at that time.</p> <p>This study is a follow-up of study 263855/004 (dTpa-004), in which healthy adolescents aged of 10 to 14 years received a dTpa booster. The purpose of this study is to evaluate in these subjects, 10 years later, the persistence of antibodies against all the vaccine antigens, and to evaluate the immunogenicity and reactogenicity of a second dTpa booster dose.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported