



Clinical trial results:

A phase IV, open, non-randomized, multicentre study to assess the reactogenicity and immunogenicity of a booster dose of GSK Biologicals' combined reduced-antigen-content diphtheria, tetanus and acellular pertussis vaccine dTpa (Boostrix™) when administered in healthy adult subjects, after previous booster vaccination with dTpa in study 263855/029 (dTpa-029).

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2009-016012-21 |
| Trial protocol | BE |
| Global end of trial date | 08 May 2012 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 |
| This version publication date | 15 April 2016 |
| First version publication date | 21 May 2015 |
| Version creation reason | • Correction of full data set Correction of sponsor name. |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 113055 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01147900 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, |
| Public contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, SKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, SKClinicalSupportHD@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 | 08 May 2012 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 May 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 May 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To assess the persistence of anti-diphtheria, anti-tetanus, anti-PT, anti-FHA, and anti-PRN antibodies 8.5 and 10 years after the previous booster dose in study 263855/029 (dTpa-029).
- To assess the immunogenicity of the administered dTpa vaccine in terms of antibody response to all vaccine antigens, one month after a second booster vaccination in subjects who will receive:
 - the Boostrix-REF vaccine and have previously received the same vaccine.
 - the Boostrix-US vaccine and have previously received the same vaccine.
 - the Boostrix-REF vaccine and have previously received the Boostrix-INV vaccine.

Protection of trial subjects:

All subjects were supervised for after 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.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 15 June 2010 |
| 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 | Belgium: 180 |
| Worldwide total number of subjects | 180 |
| EEA total number of subjects | 180 |

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) | 180 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects consisted of those previously vaccinated & boosted in GSK263855/029 study and contacted for participation in this booster (BST) study. Duration of this study was about 19 months, from Year 8.5 (8.5 years post BST in GSK263855/029 study) to one month post BST in this study (Year 10 [10 years post BST in GSK263855/029 study] + one month).

Pre-assignment

Screening details:

At Year 8.5, a total of 180 subjects (out of the 478 planned) were enrolled: 54, 60 and 66 subjects in the Boostrix-REF, Boostrix-US, and Boostrix-INV groups, respectively. At Year 10, a total of 177 subjects (out of the 180 planned) were enrolled: 55, 60 and 62 in the Boostrix-REF, Boostrix-US, and Boostrix-INV groups, respectively.

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | At Year 8.5 |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

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

| | |
|------------------|-------------------|
| Arm title | Boostrix-US Group |
|------------------|-------------------|

Arm description: -

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

Dosage and administration details:

Intramuscular, single dose

| | |
|------------------|--------------------|
| Arm title | Boostrix-INV Group |
|------------------|--------------------|

Arm description: -

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

Dosage and administration details:

Intramuscular, single dose

| | |
|------------------|--------------------|
| Arm title | Boostrix-REF Group |
|------------------|--------------------|

Arm description: -

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

Dosage and administration details:

Intramuscular, single dose

| Number of subjects in period 1 | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group |
|--------------------------------|-------------------|--------------------|--------------------|
| Started | 54 | 60 | 66 |
| Completed | 54 | 60 | 66 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | At Year 10 |
| Is this the baseline period? | Yes ^[1] |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

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

Arm description: -

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

Dosage and administration details:

Intramuscular, single dose

| | |
|------------------|--------------------|
| Arm title | Boostrix-INV Group |
|------------------|--------------------|

Arm description: -

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

Dosage and administration details:

Intramuscular, single dose

| | |
|------------------|--------------------|
| Arm title | Boostrix-REF Group |
|------------------|--------------------|

| | |
|--|-------------------|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Boostrix™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| Intramuscular, single dose | |

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: More subjects were enrolled in the second period, therefore it was considered the baseline period.

| Number of subjects in period 2^[2][3] | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group |
|--|-------------------|--------------------|--------------------|
| Started | 55 | 60 | 62 |
| Completed | 55 | 59 | 62 |
| Not completed | 0 | 1 | 0 |
| Lost to follow-up | - | 1 | - |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: More subjects enrolled in the second period of the study.

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The worldwide number enrolled was based on the first period, while the second period is the baseline.

Baseline characteristics

Reporting groups

| | |
|--------------------------------|--------------------|
| Reporting group title | Boostrix-US Group |
| Reporting group description: - | |
| Reporting group title | Boostrix-INV Group |
| Reporting group description: - | |
| Reporting group title | Boostrix-REF Group |
| Reporting group description: - | |

| Reporting group values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group |
|---|-------------------|--------------------|--------------------|
| Number of subjects | 55 | 60 | 62 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| geometric mean | 23.5 | 23.4 | 23.3 |
| standard deviation | ± 1.44 | ± 1.21 | ± 1.17 |
| Gender categorical Units: Subjects | | | |
| Female | 29 | 31 | 36 |
| Male | 26 | 29 | 26 |

| Reporting group values | Total | | |
|---|--------------------------------------|--|--|
| Number of subjects | 177 | | |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | 0 0 0 0 0 0 0 0 | | |

| | | | |
|--|----|--|--|
| Age continuous Units: years geometric mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 96 | | |
| Male | 81 | | |

End points

End points reporting groups

| | |
|--------------------------------|--------------------|
| Reporting group title | Boostrix-US Group |
| Reporting group description: - | |
| Reporting group title | Boostrix-INV Group |
| Reporting group description: - | |
| Reporting group title | Boostrix-REF Group |
| Reporting group description: - | |
| Reporting group title | Boostrix-US Group |
| Reporting group description: - | |
| Reporting group title | Boostrix-INV Group |
| Reporting group description: - | |
| Reporting group title | Boostrix-REF Group |
| Reporting group description: - | |

Primary: Number of seroprotected subjects against diphtheria and tetanus

| | |
|------------------------|--|
| End point title | Number of seroprotected subjects against diphtheria and tetanus ^[1] |
| End point description: | A subject seroprotected against diphtheria/tetanus was defined as a vaccinated subject who had an anti-diphtheria (anti-D)/anti-tetanus (anti-T) antibody concentration greater than or above (\geq) 0.1 international units per milliliter (IU/mL). |
| End point type | Primary |
| End point timeframe: | At Year 8.5 |
| Notes: | <p>[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.</p> <p>Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.</p> |

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-----------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 59 | 65 | |
| Units: Subjects | | | | |
| Anti-D | 53 | 59 | 65 | |
| Anti-T | 54 | 59 | 65 | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|------------------------|--|
| End point title | Concentrations for anti-D and anti-T antibodies. ^[2] |
| End point description: | Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of |

the assay was 0.1 IU/mL for all antibodies assessed.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| At Year 8.5 | |

Notes:

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

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

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|--|------------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 59 | 65 | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-D | 0.912 (0.728 to 1.141) | 1.205 (0.984 to 1.474) | 0.872 (0.711 to 1.068) | |
| Anti-T | 1.889 (1.585 to 2.251) | 1.991 (1.674 to 2.368) | 1.846 (1.604 to 2.123) | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against diphtheria and tetanus.

| | |
|-----------------|---|
| End point title | Number of seroprotected subjects against diphtheria and tetanus. ^[3] |
|-----------------|---|

End point description:

A subject seroprotected against diphtheria/tetanus was defined as a vaccinated subject who had an anti-D/anti-T antibody concentration greater than or above (\geq) 0.1 international units per milliliter (IU/mL).

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| At Year 10 | |

Notes:

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

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

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-----------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 60 | 61 | |
| Units: Subjects | | | | |
| Anti-D | 53 | 60 | 61 | |
| Anti-T | 54 | 60 | 61 | |

Statistical analyses

No statistical analyses for this end point

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 Year 10 | |

Notes:

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

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

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|--|-----------------------|------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 60 | 61 | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-D | 0.767 (0.6 to 0.982) | 1.099 (0.882 to 1.37) | 0.681 (0.55 to 0.844) | |
| Anti-T | 2.008 (1.65 to 2.444) | 2.009 (1.701 to 2.372) | 1.76 (1.518 to 2.041) | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-pertactin (anti-PRN) and anti-filamentous haemagglutinin (anti-FHA) antibodies.

| | |
|---|--|
| End point title | Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-pertactin (anti-PRN) and anti-filamentous haemagglutinin (anti-FHA) antibodies. ^[5] |
| End point description: A seropositive subject for anti-PT/anti-PRN/anti-FHA antibodies was defined as a vaccinated subject who had anti-PT/anti-PRN/anti-FHA antibody concentrations greater than or equal to (\geq) 5 Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). | |
| End point type | Primary |
| End point timeframe: At Year 8.5 | |

Notes:

[5] - 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-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-----------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 59 | 65 | |
| Units: Subjects | | | | |
| Anti-PT [N=54;59;65] | 42 | 48 | 60 | |
| Anti-FHA [N=54;59;62] | 54 | 59 | 62 | |
| Anti-PRN [N=54;59;65] | 54 | 59 | 65 | |

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations for anti-PT, anti-PRN and anti-FHA antibodies.

| | |
|-----------------|--|
| End point title | Concentrations for anti-PT, anti-PRN and anti-FHA antibodies. ^[6] |
|-----------------|--|

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seropositivity cut-off of the assay was 5 EL.U/mL for all antibodies assessed.

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

End point timeframe:

At Year 8.5

Notes:

[6] - 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-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|--|-----------------------------|------------------------------|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 59 | 65 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT [N=54;59;65] | 10.933 (7.979 to 14.98) | 13.372 (10.139 to 17.634) | 18.034 (13.812 to 23.545) | |
| Anti-FHA [N=54;59;62] | 72.653 (57.904 to 91.158) | 96.144 (75.613 to 122.25) | 102.604 (85.687 to 122.861) | |
| Anti-PRN [N=54;59;65] | 161.349 (121.75 to 213.827) | 179.027 (136.303 to 235.144) | 134.616 (106.266 to 170.528) | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects for anti-PT, anti-FHA and anti-PRN antibodies.

| | |
|-----------------|---|
| End point title | Number of seropositive subjects for anti-PT, anti-FHA and anti- |
|-----------------|---|

End point description:

A seropositive subject for anti-PT/anti-FHA/anti-PRN antibodies was defined as a vaccinated subject who had anti-PT/anti-FHA/anti-PRN antibody concentrations greater than or equal to (\geq) 5 Enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL).

End point type

Primary

End point timeframe:

At Year 10

Notes:

[7] - 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-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-----------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 60 | 60 | |
| Units: Subjects | | | | |
| Anti-PT [N=52;59;59] | 44 | 49 | 51 | |
| Anti-PRN [N=54;60;60] | 54 | 60 | 60 | |
| Anti-FHA [N=54;60;60] | 54 | 60 | 60 | |

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations for anti-PT, anti-FHA and anti-PRN antibodies.

End point title

Concentrations for anti-PT, anti-FHA and anti-PRN antibodies.^[8]

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

Primary

End point timeframe:

At Year 10

Notes:

[8] - 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-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|--|----------------------------|------------------------------|-----------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 60 | 60 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT [N=52;59;59] | 11.627 (8.863 to 15.252) | 13.987 (10.874 to 17.991) | 15.728 (11.76 to 21.034) | |
| Anti-PRN [N=54;60;60] | 131.814 (98.531 to 176.34) | 158.239 (120.864 to 207.171) | 115.209 (91.288 to 145.398) | |

| | | | | |
|-----------------------|---------------------------|----------------------------|---------------------------|--|
| Anti-FHA [N=54;60;60] | 75.574 (61.018 to 93.603) | 98.182 (77.166 to 124.921) | 98.441 (82.71 to 117.165) | |
|-----------------------|---------------------------|----------------------------|---------------------------|--|

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects against diphtheria and tetanus

| | |
|-----------------|--|
| End point title | Number of seroprotected subjects against diphtheria and tetanus ^[9] |
|-----------------|--|

End point description:

A subject seroprotected against diphtheria/tetanus was defined as a vaccinated subject who had an anti-D/anti-T antibody concentration greater than or above (\geq) 0.1 international units per milliliter (IU/mL).

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

End point timeframe:

At Year 10 pre booster vaccination (PRE) and at 1 month post Year 10 booster vaccination (POST)

Notes:

[9] - 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-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-----------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 59 | 60 | |
| Units: Subjects | | | | |
| Anti-D, PRE | 53 | 59 | 60 | |
| Anti-D, POST | 54 | 59 | 60 | |
| Anti-T, PRE | 54 | 59 | 60 | |
| Anti-T, POST | 54 | 59 | 60 | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Concentrations for anti-D and anti-T antibodies. ^[10] |
|-----------------|--|

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was 0.1 IU/mL for all antibodies assessed.

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

End point timeframe:

At Year 10 pre booster vaccination (PRE) and at 1 month post Year 10 booster vaccination (POST)

Notes:

[10] - 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-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|--|------------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 59 | 60 | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-D, PRE | 0.767 (0.6 to 0.982) | 1.094 (0.874 to 1.368) | 0.686 (0.552 to 0.853) | |
| Anti-D, POST | 4.251 (3.646 to 4.957) | 5.226 (4.353 to 6.275) | 4.15 (3.543 to 4.862) | |
| Anti-T, PRE | 2.008 (1.65 to 2.444) | 1.987 (1.68 to 2.35) | 1.752 (1.508 to 2.037) | |
| Anti-T, POST | 7.581 (6.523 to 8.809) | 8.456 (7.294 to 9.802) | 8.792 (7.582 to 10.195) | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects for anti-PT, anti-FHA and anti-PRN antibodies.

| | |
|-----------------|--|
| End point title | Number of seropositive subjects for anti-PT, anti-FHA and anti-PRN antibodies. ^[11] |
|-----------------|--|

End point description:

A seropositive subject for anti-PT/anti-PRN/anti-FHA antibodies was defined as a vaccinated subject who had anti-PT/anti-PRN/anti-FHA antibody concentrations greater than or equal to (\geq) 5 ELISA units per milliliter (EL.U/mL).

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

End point timeframe:

At Year 10 pre booster vaccination (PRE) and at 1 month post Year 10 booster vaccination (POST)

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

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-----------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 59 | 60 | |
| Units: Subjects | | | | |
| Anti-PT, PRE [N=52;58;58] | 44 | 48 | 50 | |
| Anti-PT, POST [N=54;59;60] | 54 | 59 | 60 | |
| Anti-PRN, PRE [N=54;59;59] | 54 | 59 | 59 | |
| Anti-PRN, POST [N=53;59;60] | 53 | 59 | 60 | |
| Anti-FHA, PRE [N=54;59;59] | 54 | 59 | 59 | |
| Anti-FHA, POST [N=53;59;60] | 53 | 59 | 60 | |

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations for anti-PT, anti-FHA and anti-PRN antibodies.

| | |
|-----------------|---|
| End point title | Concentrations for anti-PT, anti-FHA and anti-PRN |
|-----------------|---|

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 | Primary |
|----------------|---------|

End point timeframe:

At Year 10 pre booster vaccination (PRE) and at 1 month post Year 10 booster vaccination (POST)

Notes:

[12] - 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-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|--|------------------------------|------------------------------|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 59 | 60 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT, PRE [N=52;58;58] | 11.627 (8.863 to 15.252) | 14.193 (11.003 to 18.306) | 15.65 (11.643 to 21.035) | |
| Anti-PT, POST [N=54;59;60] | 82.478 (66.951 to 101.606) | 108.094 (87.703 to 133.227) | 123.964 (103.458 to 148.533) | |
| Anti-PRN, PRE [N=54;59;59] | 131.814 (98.531 to 176.34) | 161.903 (123.574 to 212.12) | 114.226 (90.201 to 144.652) | |
| Anti-PRN, POST [N=53;59;60] | 445.751 (372.77 to 533.02) | 448.475 (383.748 to 524.12) | 448.839 (379.488 to 530.863) | |
| Anti-FHA, PRE [N=54;59;59] | 75.574 (61.018 to 93.603) | 96.098 (75.507 to 122.305) | 97.698 (81.891 to 116.555) | |
| Anti-FHA, POST [N=53;59;60] | 503.532 (426.524 to 594.444) | 592.177 (516.831 to 678.507) | 558.648 (489.266 to 637.869) | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of booster responders to pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN) antigens.

| | |
|-----------------|---|
| End point title | Number of booster responders to pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN) antigens. ^[13] |
|-----------------|---|

End point description:

A booster responder to PT/PRN antigens was defined as either a vaccinated subject seronegative at analysis baseline (Year 10) with anti-PT/anti-PRN antibody concentration greater than or equal to (\geq) 5 EL.U/mL at one month post Year 10 booster vaccination, or as a vaccinated subject seropositive at analysis baseline (Year 10) and with anti-PT/anti-PRN antibody concentration with at least a 2-fold increase at one month post Year 10 booster vaccination. A seronegative/seropositive subject was defined as a vaccinated subject with anti-PT/anti-PRN antibody concentration \geq / $<$ 5 EL.U/mL.

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

End point timeframe:

At 1 month post Year 10 booster vaccination

Notes:

[13] - 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-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|--|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 46 | 52 | 52 | |
| Units: Subjects | | | | |
| Booster responses to anti-PT [N=44;51;51] | 44 | 51 | 48 | |
| Booster responses to anti-PRN [N=45;52;52] | 23 | 29 | 35 | |
| Booster responses to anti-FHA [N=46;52;50] | 43 | 47 | 48 | |

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 booster vaccination

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-----------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 55 | 59 | 62 | |
| Units: Subjects | | | | |
| Any Pain | 50 | 55 | 54 | |
| Any Redness | 23 | 23 | 21 | |
| Any Swelling | 21 | 20 | 19 | |

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 fatigue, gastrointestinal, headache and fever [defined as axillary temperature ≥ 37.5 degrees Celsius ($^{\circ}\text{C}$)]. Any = incidence of a particular symptom regardless of intensity grade and relationship to vaccination. | |
| End point type | Secondary |
| End point timeframe: | |
| During the 4-day (Days 0-3) follow-up period after booster vaccination | |

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-------------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 59 | 62 | |
| Units: Subjects | | | | |
| Any Fatigue | 17 | 20 | 22 | |
| Any Gastrointestinal Symptoms | 10 | 9 | 13 | |
| Any Headache | 13 | 19 | 13 | |
| Any Fever | 1 | 1 | 1 | |

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: | |
| An unsolicited AE is any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) 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 unsolicited AE = 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 booster vaccination

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-------------------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 55 | 60 | 62 | |
| Units: Subjects | | | | |
| Subjects with any unsolicited AE(s) | 22 | 16 | 21 | |

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, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject..

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

End point timeframe:

At Year 8.5

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-----------------------------|-------------------|--------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 54 | 60 | 66 | |
| Units: Subjects | | | | |
| Subjects with any SAE(s) | 0 | 0 | 0 | |

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, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

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

End point timeframe:

From Year 8.5 up to study end (one month post Year 10 booster vaccination)

| End point values | Boostrix-US Group | Boostrix-INV Group | Boostrix-REF Group | |
|-----------------------------|----------------------|-----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 55 | 60 | 62 | |
| Units: Subjects | | | | |
| Subjects with any SAE(s) | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs): Entire study period (From Year 8.5 to one month post Year 10) ;
Unsolicited adverse events (AEs): During the 31 days post Year 10 booster vaccination; Solicited
symptoms: During the 4 days post Year 10 booster vaccination.

Adverse event reporting additional description:

Total numbers of subjects at risk for SAEs are those at time points with highest numbers of subjects enrolled. For unsolicited and solicited AEs they correspond to the numbers of subjects with available results. Numbers at risk are the highest ones, at Year 8.5 for Boostrix-US Group, & Year 10 for the other groups.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 10 |

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Boostrix-US Group |
|-----------------------|-------------------|

Reporting group description:

Subjects in this group were healthy adult subjects aged 18 to 28 years at the time of enrolment and with previous completed primary and booster vaccination with a diphtheria-tetanus-whole cell pertussis vaccine completed by one additional booster dose of Boostrix™ vaccine, United States(US)-marketed formulation, at Day 0 in GSK 263855/029 study. These subjects received, as part of this NCT01147900 study, one further booster dose of Boostrix™ vaccine, US-marketed formulation, at Year 10, 10 years after booster vaccination in the GSK 263855/029 study. The Boostrix™ vaccine was administered intramuscularly in the deltoid muscle of the non-dominant arm.

| | |
|-----------------------|--------------------|
| Reporting group title | Boostrix-REF Group |
|-----------------------|--------------------|

Reporting group description:

Subjects in this group were healthy adult subjects aged 18 to 28 years at the time of enrolment and with previous completed primary and booster vaccination with a diphtheria-tetanus-whole cell pertussis vaccine completed by one additional booster dose of Boostrix™ vaccine, reference formulation, at Day 0 in GSK 263855/029 study. These subjects received, as part of this NCT01147900 study, one further booster dose of Boostrix™ vaccine, reference formulation, at Year 10, 10 years after booster vaccination in the GSK 263855/029 study. The Boostrix™ vaccine was administered intramuscularly in the deltoid muscle of the non-dominant arm.

| | |
|-----------------------|--------------------|
| Reporting group title | Boostrix-INV Group |
|-----------------------|--------------------|

Reporting group description:

Subjects in this group were healthy adult subjects aged 18 to 28 years at the time of enrolment and with previous completed primary and booster vaccination with a diphtheria-tetanus-whole cell pertussis vaccine completed by one additional booster dose of Boostrix™ vaccine, investigational formulation, at Day 0 in GSK 263855/029 study. These subjects received, as part of this NCT01147900 study, one further booster dose of Boostrix™ vaccine, reference formulation, at Year 10, 10 years after booster vaccination in the GSK 263855/029 study. The Boostrix™ vaccine was administered intramuscularly in the deltoid muscle of the non-dominant arm.

| Serious adverse events | Boostrix-US Group | Boostrix-REF Group | Boostrix-INV Group |
|---|-------------------|--------------------|--------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 62 (0.00%) | 0 / 60 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Boostrix-US Group | Boostrix-REF Group | Boostrix-INV Group |
|---|-------------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 50 / 55 (90.91%) | 54 / 62 (87.10%) | 55 / 60 (91.67%) |
| Nervous system disorders | | | |
| Headache (AE) | | | |
| subjects affected / exposed | 5 / 55 (9.09%) | 3 / 62 (4.84%) | 1 / 60 (1.67%) |
| occurrences (all) | 5 | 3 | 1 |
| General disorders and administration site conditions | | | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[1] | 50 / 55 (90.91%) | 54 / 62 (87.10%) | 55 / 59 (93.22%) |
| occurrences (all) | 50 | 54 | 55 |
| Redness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[2] | 23 / 55 (41.82%) | 21 / 62 (33.87%) | 23 / 59 (38.98%) |
| occurrences (all) | 23 | 21 | 23 |
| Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[3] | 21 / 55 (38.18%) | 19 / 62 (30.65%) | 20 / 59 (33.90%) |
| occurrences (all) | 21 | 19 | 20 |
| Fatigue | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[4] | 17 / 54 (31.48%) | 22 / 62 (35.48%) | 20 / 59 (33.90%) |
| occurrences (all) | 17 | 22 | 20 |
| Gastrointestinal symptoms | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[5] | 10 / 54 (18.52%) | 13 / 62 (20.97%) | 9 / 59 (15.25%) |
| occurrences (all) | 10 | 13 | 9 |
| Headache (General Symptom) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[6] | 13 / 54 (24.07%) | 13 / 62 (20.97%) | 19 / 59 (32.20%) |
| occurrences (all) | 13 | 13 | 19 |
| Infections and infestations | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 55 (10.91%) | 4 / 62 (6.45%) | 1 / 60 (1.67%) |
| occurrences (all) | 6 | 4 | 1 |

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: The number of subjects exposed consists of the number of subjects who had their 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: The number of subjects exposed consists of the number of subjects who had their 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: The number of subjects exposed consists of the number of subjects who had their 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: The number of subjects exposed consists of the number of subjects who had their 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: The number of subjects exposed consists of the number of subjects who had their 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: The number of subjects exposed consists of the number of subjects who had their symptom sheet completed.

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