

**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	v2
This version publication date	20 November 2018
First version publication date	06 June 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set• Correction of endpoint titles.

Trial information**Trial identification**

Sponsor protocol code	110806
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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
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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
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End point description:

End point type	Secondary
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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)
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End point description:

End point type	Secondary
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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
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End point description:

End point type	Secondary
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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)
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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
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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 Grade 3 solicited local symptoms

End point title	Number of subjects with any and Grade 3 solicited local symptoms
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End point description:

End point type	Secondary
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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, Grade 3 and related solicited general symptoms

End point title	Number of subjects with 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)
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End point description:

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

End point type	Secondary
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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)
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End point description:

End point type	Secondary
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.0
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Reporting groups

Reporting group title	Pooled Group
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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 who had the 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 who had the 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 who had the 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 who had the 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 who had the 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 who had the 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 who had the 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