Clinical trial results:
A phase III, open, randomised, multicentre study to assess the immunogenicity and safety of GlaxoSmithKline (GSK) Biologicals' combined reduced antigen content diphtheria-tetanus toxoids and acellular pertussis vaccine (Boostrix™) and the Chinese DT vaccine, when administered as booster vaccination in healthy children aged 6-8 years who were previously vaccinated with four doses of combined diphtheria-tetanus-pertussis (DTP) vaccine in the first two years of life.

Summary

EudraCT number	2016-000644-34
Trial protocol	Outside EU/EEA
Global end of trial date	12 May 2007

Results information

Result version number	v1 (current)
This version publication date	23 July 2016
First version publication date	23 July 2016

Trial information

Trial identification

Sponsor protocol code	108638

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00452686
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, +44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, +44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 September 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 May 2007
Global end of trial reached?	Yes
Global end of trial date	12 May 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

One month after the booster dose:
To evaluate the immunogenicity of GSK Biologicals' dTpa vaccine, in terms of antibody response to all vaccine antigens.
To assess the immunogenicity of the Chinese DT vaccine in terms of antibody response to diphtheria and tetanus toxoids

Protection of trial subjects:

The vaccinees will be observed closely for at least 30 minutes following the administration of vaccine, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 March 2007
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	China: 660
Worldwide total number of subjects	660
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	660
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Boostrix 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:

Subjects received a single booster dose of Boostrix™ vaccine as an intramuscular injection into the left deltoid muscle.

Arm title	DT Group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Chinese DT vaccine (adsorbed diphtheria and tetanus toxoid (DT) vaccine)
Investigational medicinal product code	
Other name	WIBP DT
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single booster dose of Wuhan Institute of Biological Products' (WIBP) adsorbed diphtheria and tetanus toxoid vaccine (DT) as an intramuscular injection into the left deltoid muscle.

Number of subjects in period 1	Boostrix Group	DT Group
Started	330	330
Completed	329	330
Not completed	1	0
Migrated/moved from study area	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Boostrix Group
Reporting group description: -	
Reporting group title	DT Group
Reporting group description: -	

Reporting group values	Boostrix Group	DT Group	Total
Number of subjects	330	330	660
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	6.3	6.3	
standard deviation	± 0.46	± 0.46	-
Gender categorical Units: Subjects			
Female	131	133	264
Male	199	197	396

End points

End points reporting groups

Reporting group title	Boostrix Group
Reporting group description: -	
Reporting group title	DT Group
Reporting group description: -	

Primary: Number of seroprotected subjects against anti-diphtheria (anti-D) and anti-tetanus (anti-T) antigens.

End point title	Number of seroprotected subjects against anti-diphtheria (anti-D) and anti-tetanus (anti-T) antigens.[1]

End point description:

A seroprotected subject, is a subject whose anti-D/anti-T antibody concentrations are greater than or equal to (≥) 0.1 international units per milliliter (IU/mL).

End point type	Primary

End point timeframe:

At Month 1

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 Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	162		
Units: Subjects				
Anti-D at Month 1	161	161		
Anti-T at Month 1	161	162		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with booster response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)[2]

End point description:

Booster response was defined as Anti-PT and anti-FHA antibody concentrations ≥ 20 ELISA units per millilitre (EL.U/mL), and at least a four-fold increase in anti-PRN antibody concentrations from pre-vaccination to post-vaccination time points.

End point type	Primary

End point timeframe:

At Month 1

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 Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	162		
Units: Subjects				
Anti-PT	148	22		
Anti-FHA	159	89		
Anti-PRN	135	7		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-D and anti-T antibody concentrations

End point title	Anti-D and anti-T antibody concentrations[3]

End point description:

End point type	Primary

End point timeframe:

At Month 1

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 Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	162		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D at Month 1	1.06 (0.985 to 1.141)	1.039 (0.968 to 1.116)		
Anti-T at Month 1	3.305 (3.119 to 3.502)	2.496 (2.34 to 2.663)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations[4]

End point description:

End point type	Primary

End point timeframe:

At Month 1

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 Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	162		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT at Month 1	56.7 (50.5 to 63.6)	11.9 (11 to 12.9)		
Anti-FHA at Month 1	330.8 (288.2 to 379.7)	23 (20 to 26.5)		
Anti-PRN at Month 1	168.3 (147.4 to 192.3)	14.8 (13.2 to 16.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-Pt, anti-FHA, and anti-PRN with an antibody concentration ≥20 ELISA-Units per milliliter (EL.U/mL)

End point title	Number of seropositive subjects for anti-Pt, anti-FHA, and anti-PRN with an antibody concentration ≥20 ELISA-Units per milliliter (EL.U/mL)

End point description:

End point type	Secondary

End point timeframe:

At Month 0

End point values	Boostrix Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	162		
Units: Subjects				
Anti-PT at Month 0	7	9		
Anti-FHA at Month 0	69	65		
Anti-PRN at Month 0	67	59		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects with anti-D/anti-T antibody concentrations ≥ 0.1 IU/mL

End point title	Number of seroprotected subjects with anti-D/anti-T antibody concentrations ≥ 0.1 IU/mL

End point description:

A seroprotected subject, is a subject whose anti-D/anti-T antibody concentrations are greater than or equal to (≥) 0.1 international units per millilitre (IU/mL).

End point type	Secondary

End point timeframe:

At Month 0

End point values	Boostrix Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	162		
Units: Subjects				
Anti-D at Month 0	109	117		
Anti-T at Month 0	127	135		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D/anti-T antibody concentrations

End point title	Anti-D/anti-T antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

At Month 0

End point values	Boostrix Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	162		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D at Month 0	0.109 (0.098 to 0.12)	0.115 (0.105 to 0.126)		
Anti-T at Month 0	0.199 (0.171 to 0.23)	0.23 (0.199 to 0.266)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

At Month 0

End point values	Boostrix Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	162		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT at Month 0	10.5 (10.1 to 11)	10.5 (10.2 to 10.9)		
Anti-FHA at Month 0	18.1 (16 to 20.4)	17.7 (15.7 to 19.9)		
Anti-PRN at Month 0	17.1 (15 to 19.4)	15.2 (13.5 to 17.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local and general symptoms

End point title	Number of subjects with solicited local and general symptoms

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Solicited general symptoms assessed were fatigue, fever (≥37.1 °C), gastrointestinal, headache.

End point type	Secondary

End point timeframe:
During the 4-day (Day 0-Day 3) follow-up period after the booster dose

End point values	Boostrix Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Subjects				
Pain	63	67		
Redness	49	50		
Swelling	39	28		
Fatigue	13	11		
Fever	55	45		
Gastrointestinal	11	13		
Headache	10	15		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:
During the 31-day (Day 0-Day 30) follow-up period after the booster dose

End point values	Boostrix Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Subjects				
Any AE(s)	30	40		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

End point type	Secondary

End point timeframe:

During the entire study period (from Month 0 to Month 1).

End point values	Boostrix Group	DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	330	330		
Units: Subjects				
Any SAE(s)	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local/general symptoms: During the 4-day (Day 0-Day 3) follow-up period after the booster dose. Unsolicited AE(s): During the 31-day (Day 0-Day 30) follow-up period after the booster dose. SAE(s): During the entire study period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Boostrix Group
Reporting group description: -	
Reporting group title	DT Group

Reporting group description: -

Serious adverse events	Boostrix Group	DT Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 330 (0.00%)	1 / 330 (0.30%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Food poisoning			
subjects affected / exposed	0 / 330 (0.00%)	1 / 330 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Boostrix Group	DT Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 330 (19.09%)	67 / 330 (20.30%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	63 / 330 (19.09%)	67 / 330 (20.30%)	
occurrences (all)	63	67	
Redness			

subjects affected / exposed	49 / 330 (14.85%)	50 / 330 (15.15%)	
occurrences (all)	49	50	
Swelling			
subjects affected / exposed	39 / 330 (11.82%)	28 / 330 (8.48%)	
occurrences (all)	39	28	
Fever/axillary			
subjects affected / exposed	55 / 330 (16.67%)	45 / 330 (13.64%)	
occurrences (all)	55	45	

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