Clinical trial results:
A phase IIIb, open-label, randomised, multicentre study to evaluate the immunogenicity and safety of a booster dose of GlaxoSmithKline Biologicals dTpa-IPV vaccine (Boostrix Polio) compared with Sanofi-Pasteur-MSDs DTPa-IPV (Tetravac), when co-administered with MMRV (Priorix Tetra) in 5 to 6-year-old healthy children.

Summary

EudraCT number	2008-006124-64
Trial protocol	IT
Global end of trial date	18 November 2009

Results information

Result version number	v1
This version publication date	02 May 2016
First version publication date	20 February 2015

Trial information

Trial identification

Sponsor protocol code	111815

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000500-PIP01-08
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	29 June 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 November 2009
Global end of trial reached?	Yes
Global end of trial date	18 November 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that GSK Biologicals dTpa-IPV vaccine is non-inferior to Sanofi-Pasteur-MSDs DTPa-IPV vaccine, in terms of seroprotection rates against diphtheria, tetanus and poliovirus types 1, 2 and 3, one month after vaccination.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment was always readily available in case of anaphylactic reactions following the administration of the vaccine. For this reason, the vaccinee remained under medical supervision for 30 minutes after vaccination

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 303
Worldwide total number of subjects	303
EEA total number of subjects	303

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)	303
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 Polio
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose, intramuscular administration.

Investigational medicinal product name	Priorix Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose, subcutaneously.

Arm title	Tetravac Group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Priorix Tetra
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose, subcutaneously.

Investigational medicinal product name	Tetravac
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose, intramuscular administration.

Number of subjects in period 1	Boostrix Group	Tetravac Group
Started	151	152
Completed	150	152
Not completed	1	0
Consent withdrawn by subject	1	-

Baseline characteristics

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

Reporting group values	Boostrix Group	Tetravac Group	Total
Number of subjects	151	152	303
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			
geometric mean	5	5	
standard deviation	± 0.14	± 0.14	-
Gender categorical Units: Subjects			
Female	81	68	149
Male	70	84	154

End points

End points reporting groups

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

Primary: Anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentrations

End point title	Anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentrations[1]
End point description:	
End point type	Primary
End point timeframe:	
At 1 Month post-vaccination	

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	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D	9.207 (8.057 to 10.522)	21.393 (19.165 to 23.88)		
Anti-T	12.527 (10.957 to 14.323)	11.07 (9.872 to 12.413)		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-poliovirus types 1, 2 and 3 antibody titres

End point title	Anti-poliovirus types 1, 2 and 3 antibody titres[2]
End point description:	
End point type	Primary
End point timeframe:	
At 1 Month post-vaccination	

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	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-poliovirus type 1	1145.6 (978.7 to 1340.9)	948 (817.5 to 1099.4)		
Anti-poliovirus type 2	1076.4 (908.7 to 1274.9)	1315.3 (1123.1 to 1540.3)		
Anti-poliovirus type 3	1937.8 (1631.4 to 2301.8)	1657.3 (1385.5 to 1982.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentrations above 0.1 IU/mL.

End point title	Number of subjects with anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibody concentrations above 0.1 IU/mL.[3]

End point description:

End point type	Primary

End point timeframe:

At 1 Month post-vaccination

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	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Subjects				
Anti-D	139	144		
Anti-T	139	144		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-poliovirus types 1, 2 and 3 antibody titres above 8

End point title	Number of subjects with anti-poliovirus types 1, 2 and 3 antibody titres above 8[4]

End point description:

End point type	Primary

End point timeframe:

At 1 Month post-vaccination

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	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Subjects				
Anti-poliovirus type 1	139	144		
Anti-poliovirus type 2	139	144		
Anti-poliovirus type 3	138	144		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT	59.8 (52.2 to 68.5)	75.9 (65.7 to 87.7)		

Anti-FHA	556.2 (491.4 to 629.5)	613.5 (547 to 688.2)		
Anti-PRN	354.8 (280.2 to 449.4)	7.8 (6.5 to 9.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-D and anti-T antibody concentrations ≥ 1.0 IU/mL

End point title	Number of subjects with anti-D and anti-T antibody concentrations ≥ 1.0 IU/mL

End point description:

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Subjects				
Anti-D	138	137		
Anti-T	144	143		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-measles, anti-mumps, anti-rubella and anti-varicella antibody titres above the cut-off values

End point title	Number of subjects with anti-measles, anti-mumps, anti-rubella and anti-varicella antibody titres above the cut-off values

End point description:

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	146		
Units: Subjects				
Anti- measles	139	146		
Anti-mumps	139	144		
Anti-rubella	139	146		
Anti- varicella	135	140		

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 1 Month post-vaccination

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT	59.8 (52.2 to 68.5)	75.9 (65.7 to 87.7)		
Anti-FHA	556.2 (491.4 to 629.5)	613.5 (547 to 688.2)		
Anti-PRN	354.8 (280.2 to 449.4)	7.8 (6.5 to 9.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-measles, anti-mumps, anti-rubella and anti-varicella antibody titres

End point title	Anti-measles, anti-mumps, anti-rubella and anti-varicella antibody titres

End point description:

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	146		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti- measles	2743.9 (2411.4 to 3122.2)	2863 (2534.6 to 3233.9)		
Anti-mumps	4141.3 (3590.5 to 4776.5)	3837.6 (3275.1 to 4496.7)		
Anti-rubella	154.5 (141.3 to 168.9)	162.5 (145.8 to 181)		
Anti- varicella	856.7 (671.8 to 1092.4)	909.9 (721 to 1148.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster responses for anti-diphtheria and anti-tetanus antibody concentrations

End point title	Number of subjects with booster responses for anti-diphtheria and anti-tetanus antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	143		
Units: Subjects				
Anti-D	130	136		
Anti-T	137	142		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster responses for anti-poliovirus types 1, 2 and 3 antibody concentrations

End point title	Number of subjects with booster responses for anti-poliovirus types 1, 2 and 3 antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	144		
Units: Subjects				
Anti-poliovirus type 1	115	112		
Anti-poliovirus type 2	113	112		
Anti-poliovirus type 3	126	127		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster responses for anti-PT, anti-FHA and anti-PRN antibody concentrations

End point title	Number of subjects with booster responses for anti-PT, anti-FHA and anti-PRN antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	143		
Units: Subjects				
Anti-PT	123	130		
Anti-FHA	129	134		
Anti-PRN	129	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for anti-measles, anti-mumps, anti-rubella and anti-varicella

End point title	Number of seroconverted subjects for anti-measles, anti-mumps, anti-rubella and anti-varicella

End point description:

End point type	Secondary

End point timeframe:

At 1 Month post-vaccination

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	34		
Units: Subjects				
Anti- measles	2	1		
Anti-mumps	13	12		
Anti-rubella	0	0		
Anti- varicella	35	32		

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:

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	152		
Units: Subjects				
Pain	96	96		
Redness	58	66		
Swelling	55	62		

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:

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	152		
Units: Subjects				
Fatigue	40	36		
Gastrointestinal	23	15		
Headache	18	20		
Temperature	32	30		

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:

End point type	Secondary

End point timeframe:

During the 31 days (Days 0-30) post-vaccination period

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	152		
Units: Subjects				
Subjects with any AE(s)	23	20		

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 whole study period

End point values	Boostrix Group	Tetravac Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	152		
Units: Subjects				
Subjects with any SAE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: 4-day follow-up period after vaccination (Day 0 - Day 3); Unsolicited AEs: 31-day follow-up period after vaccination (Day 0 - Day 30); SAEs: throughout the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13

Reporting groups

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

Reporting group description: -

Serious adverse events	Boostrix Group	Tetravac Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 151 (0.00%)	0 / 152 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Boostrix Group	Tetravac Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	96 / 151 (63.58%)	96 / 152 (63.16%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	96 / 151 (63.58%)	96 / 152 (63.16%)	
occurrences (all)	96	96	
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 151 (15.23%)	15 / 152 (9.87%)	
occurrences (all)	23	15	
Headache			

alternative assessment type: Systematic			
subjects affected / exposed	18 / 151 (11.92%)	20 / 152 (13.16%)	
occurrences (all)	18	20	
Temperature			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 151 (21.19%)	30 / 152 (19.74%)	
occurrences (all)	32	30	
Gastrointestinal disorders			
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	58 / 151 (38.41%)	66 / 152 (43.42%)	
occurrences (all)	58	66	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	55 / 151 (36.42%)	62 / 152 (40.79%)	
occurrences (all)	55	62	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	40 / 151 (26.49%)	36 / 152 (23.68%)	
occurrences (all)	40	36	

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