Clinical trial results:
An open-label study to assess the immunogenicity and reactogenicity of GlaxoSmithKline (GSK) Biologicals' IPV vaccine (Poliorix) administered as a booster dose at 18 months of age in healthy Chinese toddlers previously primed with the same vaccine in the study IPV-018 (NCT01323647).

Summary

EudraCT number	2012-004513-14
Trial protocol	Outside EU/EEA
Global end of trial date	19 September 2011

Results information

Result version number	v1
This version publication date	08 April 2016
First version publication date	12 July 2015

Trial information

Trial identification

Sponsor protocol code	114306

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01323647
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 September 2011
Global end of trial reached?	Yes
Global end of trial date	19 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To assess the immunological response to a booster dose of GSK Biologicals' IPV in terms of poliovirus type 1, 2 and 3 antibodies, one month after the booster dose in subjects primed with three doses of the same IPV in study IPV-018.
• To assess the persistence of antibodies to poliovirus types 1, 2 and 3 antigens at 18 months of age in subjects primed with three doses of GSK Biologicals' IPV or three doses of OPV in study IPV-018.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 2011
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: 957
Worldwide total number of subjects	957
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)	957
Children (2-11 years)	0
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	IPV Group

Arm description:

Subjects previously primed with 3 doses of IPV vaccine in the primary study and who received a booster dose of IPV vaccine co-administered with DTPa/Hib vaccine in the current study.

Arm type	Experimental
Investigational medicinal product name	Poliorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered intramuscularly into the anterolateral side of the thigh.

Investigational medicinal product name	Infanrix-Hib™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose administered intramuscularly into the anterolateral side of the thigh. Part of the local standard of care. No outcome measures associated.

Arm title	Control Group

Arm description:

Subjects previously primed with 3 doses of Chinese OPV vaccine in the primary study and who received a dose of DTPa/Hib vaccine in the current study.

Arm type	Active comparator
Investigational medicinal product name	Poliorix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered intramuscularly into the anterolateral side of the thigh.

Investigational medicinal product name	Infanrix-Hib™
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose administered intramuscularly into the anterolateral side of the thigh. Part of the local standard of care. No outcome measures associated.

Number of subjects in period 1	IPV Group	Control Group
Started	470	487
Completed	461	487
Not completed	9	0
Consent withdrawn by subject	5	-
Migrated/moved from study area	2	-
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	IPV Group
Reporting group description:	
Subjects previously primed with 3 doses of IPV vaccine in the primary study and who received a booster dose of IPV vaccine co-administered with DTPa/Hib vaccine in the current study.	
Reporting group title	Control Group
Reporting group description:	
Subjects previously primed with 3 doses of Chinese OPV vaccine in the primary study and who received a dose of DTPa/Hib vaccine in the current study.	

Reporting group values	IPV Group	Control Group	Total
Number of subjects	470	487	957
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: months			
arithmetic mean	18.7	18.8	
standard deviation	± 0.93	± 1.01	-
Gender categorical			
Units: Subjects			
Female	234	227	461
Male	236	260	496

End points

End points reporting groups

Reporting group title	IPV Group
Reporting group description:	
Subjects previously primed with 3 doses of IPV vaccine in the primary study and who received a booster dose of IPV vaccine co-administered with DTPa/Hib vaccine in the current study.	
Reporting group title	Control Group
Reporting group description:	
Subjects previously primed with 3 doses of Chinese OPV vaccine in the primary study and who received a dose of DTPa/Hib vaccine in the current study.	

Primary: Number of subjects seroprotected for poliovirus types 1, 2 and 3 antibodies above the cut-off value.

End point title	Number of subjects seroprotected for poliovirus types 1, 2 and 3 antibodies above the cut-off value.[1][2]
End point description:	
A seroprotected subject was defined as a vaccinated subject whose antibody titer is greater than or equal to (≥) 8 ED50. This outcome measure concerns subjects in the IPV Group only.	
End point type	Primary
End point timeframe:	
One month after IPV booster 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.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns subjects in the IPV Group only.

End point values	IPV Group			
Subject group type	Reporting group			
Number of subjects analysed	456			
Units: Subjects				
Anti-poliovirus 1	456			
Anti-poliovirus 2	456			
Anti-poliovirus 3	456			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects seroprotected for poliovirus types 1, 2 and 3 antibodies above the cut-off value.

End point title	Number of subjects seroprotected for poliovirus types 1, 2 and 3 antibodies above the cut-off value.[3]
End point description:	
A seroprotected subject was defined as a vaccinated subject whose antibody titer is greater than or	

equal to (≥) 8 ED50.

End point type	Primary

End point timeframe:

Before booster 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	IPV Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263	280		
Units: Subjects				
Anti-poliovirus 1	263	280		
Anti-poliovirus 2	263	280		
Anti-poliovirus 3	263	276		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody titres against poliovirus type 1, 2 and 3.

End point title	Antibody titres against poliovirus type 1, 2 and 3.[4][5]

End point description:

Antibody titers were summarized by geometric mean titers (GMTs) with their 95% CIs. This outcome measure concerns subjects in the IPV Group only.

End point type	Primary

End point timeframe:

One month after IPV booster 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.
[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns subjects in the IPV Group only.

End point values	IPV Group			
Subject group type	Reporting group			
Number of subjects analysed	456			
Units: Titres				
geometric mean (confidence interval 95%)				
Anti-poliovirus 1	3420.8 (3153.8 to 3710.5)			
Anti-poliovirus 2	1886.8 (1732.7 to 2054.5)			
Anti-poliovirus 3	5097 (4706.8 to 5519.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Antibody titres against poliovirus type 1, 2 and 3.

End point title	Antibody titres against poliovirus type 1, 2 and 3.[6]

End point description:

Antibody titers were summarized by geometric mean titers (GMTs) with their 95% CIs.

End point type	Primary

End point timeframe:

Before booster vaccination.

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	IPV Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	263	280		
Units: Titres				
geometric mean (confidence interval 95%)				
Anti-poliovirus 1	494.4 (441.6 to 553.6)	2747.1 (2411.3 to 3129.6)		
Anti-poliovirus 2	239.4 (211.5 to 270.9)	464.7 (411.1 to 525.2)		
Anti-poliovirus 3	819.8 (713.6 to 941.9)	415.2 (356.1 to 484.2)		

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.[7]

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 pain = Cry when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site. This outcome measure concerns subjects in the IPV Group only.

End point type	Secondary

End point timeframe:

Within 4-days (Days 0-3) post IPV booster vaccination.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns subjects in the IPV Group only.

End point values	IPV Group			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: Subjects				
Any Pain	49			
Grade 3 Pain	3			
Any Redness	22			
Grade 3 Redness	0			
Any Swelling	11			
Grade 3 Swelling	0			

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.[8]

End point description:

Solicited general symptoms assessed include drowsiness, irritability, loss of appetite and fever (defined as axillary temperature ≥37.0°C). Any was defined as incidence of the specified symptoms regardless of intensity or relationship to study vaccine. Grade 3 drowsiness was defined as drowsiness that prevents normal activities. Grade 3 fever was defined as fever (axillary temperature) >39.0°C. Grade 3 irritability was defined as crying more than usual/ interferes with normal activities. Grade 3 loss of appetite was defined as not eating at all. Related = symptom assessed by the investigator as related to the vaccination. This outcome measure concerns subjects only in the IPV Group.

End point type	Secondary

End point timeframe:

Within 4-days (Days 0-3) post IPV booster vaccination.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns subjects only in the IPV Group.

End point values	IPV Group			
Subject group type	Reporting group			
Number of subjects analysed	467			
Units: Subjects				
Any Drowsiness	59			
Grade 3 Drowsiness	1			
Related Drowsiness	59			
Any Irritability	86			
Grade 3 Irritability	2			

Related Irritability	84			
Any Loss of appetite	84			
Grade 3 Loss of appetite	1			
Related Loss of appetite	83			
Any temperature	156			
Grade 3 temperature	8			
Related temperature	153			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse event (AE).

End point title	Number of subjects reporting any unsolicited adverse event (AE).[9]

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Any solicited symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event. This outcome measure concerns subjects in the IPV Group only.

End point type	Secondary

End point timeframe:

Within the 31-day follow-up period after the IPV booster vaccination.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns subjects in the IPV Group only.

End point values	IPV Group			
Subject group type	Reporting group			
Number of subjects analysed	470			
Units: Subjects				
Any AE(s)	22			

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:

Serious adverse events (SAEs) assessed include medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity.

End point type	Secondary

End point timeframe:

During the entire study period (Day 0 to Month 01).

End point values	IPV Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	470	451		
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:

Serious Adverse Events: during the entire study period (Day 0 to Month 01); Solicited local and general symptoms: during the 4-day (Days 0-3) post-booster vaccination period; Unsolicited symptoms: within 31 days after IPV booster vaccination.

Adverse event reporting additional description:

The number of occurrences reported for solicited symptoms, adverse events, and serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	IPV Group

Reporting group description:

Subjects previously primed with 3 doses of IPV vaccine in the primary study and who received a booster dose of IPV vaccine co-administered with DTPa/Hib vaccine in the current study.

Reporting group title	Control Group

Reporting group description:

Subjects previously primed with 3 doses of Chinese OPV vaccine in the primary study and who received a dose of DTPa/Hib vaccine in the current study.

Serious adverse events	IPV Group	Control Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 470 (0.00%)	1 / 451 (0.22%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 470 (0.00%)	1 / 451 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	IPV Group	Control Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	156 / 470 (33.19%)	0 / 451 (0.00%)	

General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	49 / 467 (10.49%)	0 / 451 (0.00%)	
occurrences (all)	49	0	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	59 / 467 (12.63%)	0 / 451 (0.00%)	
occurrences (all)	59	0	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[3]	86 / 467 (18.42%)	0 / 451 (0.00%)	
occurrences (all)	86	0	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[4]	84 / 467 (17.99%)	0 / 451 (0.00%)	
occurrences (all)	84	0	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[5]	156 / 467 (33.40%)	0 / 451 (0.00%)	
occurrences (all)	156	0	

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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms included only doses with documented safety data (i.e. symptom screen 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: For a given subject and for the analysis of solicited symptom within 4 days post-vaccination, missing or non-evaluable measurements were not replaced. Therefore the analysis of the

solicited symptoms included only doses with documented safety data (i.e. symptom screen 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