Clinical trial results:
Immunogenicity and Safety of Fractional Booster Dose of sanofi pasteur's Inactivated Poliomyelitis Vaccine (IMOVAX Polio) Administered Intradermally versus Full Booster Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio) Administered Intramuscularly at 15 to 18 Months of Age in Healthy Toddlers in The Philippines

Summary

EudraCT number	2015-005184-16
Trial protocol	Outside EU/EEA
Global end of trial date	28 July 2009

Results information

Result version number	v1 (current)
This version publication date	16 April 2016
First version publication date	16 April 2016

Trial information

Trial identification

Sponsor protocol code	IPV26

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00885157
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon cedex 07, France, F-69367
Public contact	Franchise Medical Director, Sanofi Pasteur SA, 33 4 37 65 67 99, Emmanuel.Vidor@sanofipasteur.com
Scientific contact	Franchise Medical Director, Sanofi Pasteur SA, 33 4 37 65 67 99, Emmanuel.Vidor@sanofipasteur.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	11 January 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 July 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To describe in each group the immunogenicity of IMOVAX Polio administered intradermally or intramuscularly, one month after the booster dose given at 15-18 months of age in toddlers previously primed with three doses of IMOVAX Polio vaccine during the IPV25 study

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

This study was designed to assess the immunogenicity and safety of a fractional booster dose of IMOVAX Polio administered intradermally, compared to a full booster dose of IMOVAX Polio administered intramuscularly, at 15 to 18 months of age, after a three-dose primary vaccination series during the IPV25 study.

Evidence for comparator:

Not applicable

Actual start date of recruitment	07 April 2009
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	Philippines: 225
Worldwide total number of subjects	225
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)	225

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:

Study subjects were enrolled from 07 April 2009 to 25 June 2009 at 1 clinic center in the Philippines.

Pre-assignment

Screening details:

A total of 225 subjects who met all inclusion and none of the exclusion criteria were enrolled and vaccinated in this study.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Fractional Dose of IMOVAX Polio™

Arm description:

Toddlers received Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally as primary vaccination series (IPV25) and received a fractional booster dose (0.1 mL or 1/5 of full dose) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally between 15 and 18 months of age. Toddlers also received concomitant DTw-Hib vaccine (TETRAct-HIb®) between 12 and 24 months of age.

Arm type	Experimental
Investigational medicinal product name	IPV (IMOVAX Polio™)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intradermal use

Dosage and administration details:

0.1 mL, intradermal into the right upper arm using the Mantoux technique, 1 booster dose.

Arm title	Full Dose of IMOVAX Polio™

Arm description:

Toddlers received Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intramuscularly as primary vaccination series (IPV25) and received a full booster dose (0.5mL) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intramuscularly between 15 and 18 months of age. Toddlers also received concomitant DTw-Hib vaccine (TETRAct-HIb®) between 12 and 24 months of age.

Arm type	Active comparator
Investigational medicinal product name	IPV (IMOVAX Polio™)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intradermal into the anterolateral, 1 booster dose.

Number of subjects in period 1	Fractional Dose of IMOVAX Polio™	Full Dose of IMOVAX Polio™
Started	113	112
Completed	113	111
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Fractional Dose of IMOVAX Polio™

Reporting group description:

Toddlers received Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally as primary vaccination series (IPV25) and received a fractional booster dose (0.1 mL or 1/5 of full dose) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally between 15 and 18 months of age. Toddlers also received concomitant DTw-Hib vaccine (TETRAct-HIb®) between 12 and 24 months of age.

Reporting group title	Full Dose of IMOVAX Polio™

Reporting group description:

Toddlers received Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intramuscularly as primary vaccination series (IPV25) and received a full booster dose (0.5mL) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intramuscularly between 15 and 18 months of age. Toddlers also received concomitant DTw-Hib vaccine (TETRAct-HIb®) between 12 and 24 months of age.

Reporting group values	Fractional Dose of IMOVAX Polio™	Full Dose of IMOVAX Polio™	Total
Number of subjects	113	112	225
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	113	112	225
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
arithmetic mean	15.8	15.8	
standard deviation	± 0.7	± 0.8	-
Gender categorical Units: Subjects			
Female	55	70	125
Male	58	42	100

End points

End points reporting groups

Reporting group title	Fractional Dose of IMOVAX Polio™

Reporting group description:

Toddlers received Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally as primary vaccination series (IPV25) and received a fractional booster dose (0.1 mL or 1/5 of full dose) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally between 15 and 18 months of age. Toddlers also received concomitant DTw-Hib vaccine (TETRAct-HIb®) between 12 and 24 months of age.

Reporting group title	Full Dose of IMOVAX Polio™

Reporting group description:

Toddlers received Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intramuscularly as primary vaccination series (IPV25) and received a full booster dose (0.5mL) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intramuscularly between 15 and 18 months of age. Toddlers also received concomitant DTw-Hib vaccine (TETRAct-HIb®) between 12 and 24 months of age.

Primary: Percentage of Infant Subjects with Anti-Poliovirus 1, 2 and 3 Titers of 1 ≥4 (1/dil) or 1 ≥8 (1/dil) Before and Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)

End point title	Percentage of Infant Subjects with Anti-Poliovirus 1, 2 and 3 Titers of 1 ≥4 (1/dil) or 1 ≥8 (1/dil) Before and Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)[1]

End point description:

Anti-Poliovirus types 1, 2, and 3 were measured by neutralization assay.

End point type	Primary

End point timeframe:

Pre- and Post-booster

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Fractional Dose of IMOVAX Polio™	Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	111		
Units: Percentage of subjects				
number (not applicable)				
Anti-Polio 1; Pre-Booster; ≥ 4 (1/dil)	100	100		
Anti-Polio 1; Post-Booster; ≥ 4 (1/dil)	100	100		
Anti-Polio 1; Pre-Booster; ≥ 8 (1/dil)	95.5	100		
Anti-Polio 1; Post-Booster; ≥ 8 (1/dil)	100	100		
Anti-Polio 2; Pre-Booster; ≥ 4 (1/dil)	98.2	100		
Anti-Polio 2; Post-Booster; ≥ 4 (1/dil)	100	100		
Anti-Polio 2; Pre-Booster; ≥ 8 (1/dil)	95.5	98.2		
Anti-Polio 2; Post-Booster; ≥ 8 (1/dil)	100	100		
Anti-Polio 3; Pre-Booster; ≥ 4 (1/dil)	97.3	99.1		

Anti-Polio 3; Post-Booster; ≥ 4 (1/dil)	100	100		
Anti-Polio 3; Pre-Booster; ≥ 8 (1/dil)	88.3	96.4		
Anti-Polio 3; Post-Booster; ≥ 8 (1/dil)	100	100		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers of Anti-Polio 1, 2, and 3 Antibodies Before and Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)

End point title	Geometric Mean Titers of Anti-Polio 1, 2, and 3 Antibodies Before and Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)[2]

End point description:

Anti-Poliovirus types 1, 2, and 3 were measured by neutralization assay.

End point type	Primary

End point timeframe:

Pre- and Post-booster

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Fractional Dose of IMOVAX Polio™	Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	111		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Polio 1; Pre-Booster	48.2 (38.7 to 59.9)	109.8 (84.3 to 143.2)		
Anti-Polio 1; Post-Booster	2833.7 (2392.2 to 3356.7)	6666.5 (5613.7 to 7916.6)		
Anti-Polio 2; Pre-Booster	94 (65.8 to 134.2)	132.5 (98.4 to 178.3)		
Anti-Polio 2; Post-Booster	3210.7 (2672.5 to 3857.1)	6522.3 (5540.6 to 7678.1)		
Anti-Polio 3; Pre-Booster	50.3 (37.6 to 67.4)	136.7 (103 to 181.3)		
Anti-Polio 3; Post-Booster	4498.2 (3608.3 to 5607.5)	11952.7 (10046.8 to 14220.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titer Ratios of Anti-Polio 1, 2, and 3 Antibodies Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)

End point title	Geometric Mean Titer Ratios of Anti-Polio 1, 2, and 3 Antibodies Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)[3]

End point description:

Anti-Poliovirus types 1, 2, and 3 were measured by neutralization assay.

End point type	Primary

End point timeframe:

Post-/Pre-Booster

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Fractional Dose of IMOVAX Polio™	Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	111		
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Polio 1	58.8 (44.9 to 77)	60.7 (45.7 to 80.7)		
Anti-Polio 2	34.2 (23.9 to 48.9)	49.2 (35.1 to 69)		
Anti-Polio 3	89.4 (62.8 to 127.1)	87.4 (63.2 to 121)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Infant Subjects with ≥4-fold increase of Anti-Polio 1, 2, and 3 Antibodies Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)

End point title	Percentage of Infant Subjects with ≥4-fold increase of Anti-Polio 1, 2, and 3 Antibodies Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)[4]

End point description:

Anti-Poliovirus types 1, 2, and 3 were measured by neutralization assay.

End point type	Primary

End point timeframe:

Post-booster

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Fractional Dose of IMOVAX Polio™	Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	111		
Units: Percentage of subjects				
number (not applicable)				
Anti-Polio 1	95.5	96.4		
Anti-Polio 2	83.8	88.3		
Anti-Polio 3	94.6	94.6		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Infant Subjects with Solicited Injection-site and Systemic Reactions Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)

End point title	Percentage of Infant Subjects with Solicited Injection-site and Systemic Reactions Following Vaccination with Either A Fractional Booster-Dose Or A Full Booster-Dose of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)[5]

End point description:

Solicited Injection site reactions: Tenderness, Erythema, Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, Irritability.

Grade 3 Solicited Injection site reactions: Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥ 5 cm. Grade 3 Solicited systemic reactions: Fever, > 39.5°C; Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, > 3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refuses ≥ 3 feeds/meals or refuses most feeds/meals; Irritability, Inconsolable.

End point type	Primary

End point timeframe:

Day 0 to Day 7 post-booster

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Fractional Dose of IMOVAX Polio™	Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	112		
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Tenderness	28.6	21.2		
Grade 3 Injection site Tenderness	0	0		

Any Injection site Erythema	38.4	11.5		
Grade 3 Injection site Erythema	0	0		
Any Injection site Swelling	8.9	1.8		
Grade 3 Injection site Swelling	0	0		
Any Fever	8	15		
Grade 3 Fever	0.9	0.9		
Any Vomiting	3.6	5.3		
Grade 3 Vomiting	0	0		
Any Crying abnormal	2.7	3.5		
Grade 3 Crying abnormal	0	0		
Any Drowsiness	5.4	8		
Grade 3 Drowsiness	0	0		
Any Appetite lost	8	7.1		
Grade 3 Appetite lost	0	0		
Any Irritability	6.3	9.7		
Grade 3 Irritability	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 up to Day 7 post-booster vaccine injection.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Fractional Dose of IMOVAX Polio™

Reporting group description:

Toddlers received Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally as primary vaccination series (IPV25) and received a fractional booster dose (0.1 mL or 1/5 of full dose) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally between 15 and 18 months of age. Toddlers also received concomitant DTw-Hib vaccine (TETRAct-HIb®) between 12 and 24 months of age.

Reporting group title	Full Dose of IMOVAX Polio™

Reporting group description:

Toddlers received Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intramuscularly as primary vaccination series (IPV25) and received a full booster dose (0.5mL) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intramuscularly between 15 and 18 months of age. Toddlers also received concomitant DTw-Hib vaccine (TETRAct-HIb®) between 12 and 24 months of age.

Serious adverse events	Fractional Dose of IMOVAX Polio™	Full Dose of IMOVAX Polio™	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 112 (0.00%)	2 / 112 (1.79%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	0 / 112 (0.00%)	2 / 112 (1.79%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fractional Dose of IMOVAX Polio™	Full Dose of IMOVAX Polio™	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 112 (49.11%)	36 / 112 (32.14%)	
Nervous system disorders			

Any Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 112 (5.36%)	9 / 112 (8.04%)	
occurrences (all)	6	9	
General disorders and administration site conditions			
Any Injection site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 112 (28.57%)	24 / 112 (21.43%)	
occurrences (all)	32	24	
Any Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	43 / 112 (38.39%)	13 / 112 (11.61%)	
occurrences (all)	43	13	
Any Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 112 (8.93%)	2 / 112 (1.79%)	
occurrences (all)	10	2	
Any Fever			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 112 (8.04%)	17 / 112 (15.18%)	
occurrences (all)	9	17	
Gastrointestinal disorders			
Any Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 112 (3.57%)	6 / 112 (5.36%)	
occurrences (all)	4	6	
Psychiatric disorders			
Any Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 112 (6.25%)	11 / 112 (9.82%)	
occurrences (all)	7	11	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	34 / 112 (30.36%)	36 / 112 (32.14%)	
occurrences (all)	41	42	
Metabolism and nutrition disorders			

Any Appetite lost			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 112 (8.04%)	8 / 112 (7.14%)	
occurrences (all)	9	8	

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