Clinical trial results:
Immunogenicity and Safety of different sequential schedules of Inactivated Poliomyelitis Vaccine (IMOVAX Polio®) followed by Oral Poliomyelitis Vaccine in Healthy Infants in China versus Oral Poliomyelitis Vaccine Alone

Summary

EudraCT number	2015-005188-17
Trial protocol	Outside EU/EEA
Global end of trial date	24 June 2013

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	IPV30

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01475539
WHO universal trial number (UTN)	U1111-1122-1928

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur China
Sponsor organisation address	6th floor, No. 112 Jian Guo Lu, Chaoyang District, Beijing, China, 100022
Public contact	Director, Medical Affairs, Sanofi Pasteur China, 86 10 6568 5588, Jean-denis.shu@sanofipasteur.com
Scientific contact	Director, Medical Affairs, Sanofi Pasteur China, 86 10 6568 5588, Jean-denis.shu@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	29 May 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 June 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To demonstrate the non-inferiority of Inactivated Poliomyelitis Vaccine (IPV)-(Oral Poliomyelitis Vaccine) (OPV)-OPV (Sequential 1) and IPV-IPV-OPV (sequential 2) poliovirus vaccine administrations versus OPV-OPV-OPV (Reference) in terms of seroprotection rate 28 to 42 days after the third dose of the primary vaccination series.

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:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	07 November 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: 456
Worldwide total number of subjects	456
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)	456
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 November 2011 to 16 February 2012 at 1 clinic center in China.

Pre-assignment

Screening details:

A total of 456 subjects met all inclusion and none of the exclusion criteria and were enrolled and vaccinated in the 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	IPV-OPV-OPV (Sequential 1)

Arm description:

Infants ≥ 2 months and under 3 months of age sequentially received Sanofi Pasteur's injectable Inactivated Poliovirus Vaccine (IPV; IMOVAX Polio™) at 2 months and commercially available Oral Poliovirus Vaccine (OPV) at 3 and 4 months of age.

Arm type	Experimental
Investigational medicinal product name	IMOVAX Polio, injectable Inactivated Poliovirus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular into the anterolateral area of the thigh, 1 injection at 2 months of age

Investigational medicinal product name	Poliomyelitis Vaccine in Dragee Candy (Monkey Kidney Cell), Live (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 g dragee, oral, 1 administration each at 3 and 4 months of age

Arm title	IPV-IPV-OPV (Sequential 2)

Arm description:

Infants ≥ 2 months and under 3 months of age sequentially received Sanofi Pasteur's injectable Inactivated Poliovirus Vaccine (IPV; IMOVAX Polio™) at 2 and 3 months and commercially available Oral Poliovirus Vaccine (OPV) at 4 months of age.

Arm type	Experimental
Investigational medicinal product name	IMOVAX Polio, injectable Inactivated Poliovirus vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:	
0.5 mL, intramuscular into the anterolateral area of the thigh, 1 injection each at 2 and 3 months of age	
Investigational medicinal product name	Poliomyelitis Vaccine in Dragee Candy (Monkey Kidney Cell), Live (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
1 g dragee, oral, 1 administration at 4 months of age	
Arm title	OPV-OPV-OPV (Control)
Arm description:	
Infants ≥ 2 months and under 3 months of age sequentially received commercially available Oral Poliovirus Vaccine (OPV) at 2, 3, and 4 months of age.	
Arm type	Active comparator
Investigational medicinal product name	Poliomyelitis Vaccine in Dragee Candy (Monkey Kidney Cell), Live (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
1 g dragee, oral, 1 administration each at 2, 3, and 4 months of age	

Number of subjects in period 1	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)
Started	152	152	152
Completed	148	150	149
Not completed	4	2	3
Consent withdrawn by subject	4	2	2
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	IPV-OPV-OPV (Sequential 1)
Reporting group description:	
Infants ≥ 2 months and under 3 months of age sequentially received Sanofi Pasteur's injectable Inactivated Poliovirus Vaccine (IPV; IMOVAX Polio™) at 2 months and commercially available Oral Poliovirus Vaccine (OPV) at 3 and 4 months of age.	
Reporting group title	IPV-IPV-OPV (Sequential 2)
Reporting group description:	
Infants ≥ 2 months and under 3 months of age sequentially received Sanofi Pasteur's injectable Inactivated Poliovirus Vaccine (IPV; IMOVAX Polio™) at 2 and 3 months and commercially available Oral Poliovirus Vaccine (OPV) at 4 months of age.	
Reporting group title	OPV-OPV-OPV (Control)
Reporting group description:	
Infants ≥ 2 months and under 3 months of age sequentially received commercially available Oral Poliovirus Vaccine (OPV) at 2, 3, and 4 months of age.	

Reporting group values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)
Number of subjects	152	152	152
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)	152	152	152
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	2.5	2.5	2.5
standard deviation	± 0.3	± 0.3	± 0.3
Gender categorical Units: Subjects			
Female	71	70	78
Male	81	82	74

Reporting group values	Total		
Number of subjects	456		
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)	456		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	219		
Male	237		

End points

End points reporting groups

Reporting group title	IPV-OPV-OPV (Sequential 1)
Reporting group description:	
Infants ≥ 2 months and under 3 months of age sequentially received Sanofi Pasteur's injectable Inactivated Poliovirus Vaccine (IPV; IMOVAX Polio™) at 2 months and commercially available Oral Poliovirus Vaccine (OPV) at 3 and 4 months of age.	
Reporting group title	IPV-IPV-OPV (Sequential 2)
Reporting group description:	
Infants ≥ 2 months and under 3 months of age sequentially received Sanofi Pasteur's injectable Inactivated Poliovirus Vaccine (IPV; IMOVAX Polio™) at 2 and 3 months and commercially available Oral Poliovirus Vaccine (OPV) at 4 months of age.	
Reporting group title	OPV-OPV-OPV (Control)
Reporting group description:	
Infants ≥ 2 months and under 3 months of age sequentially received commercially available Oral Poliovirus Vaccine (OPV) at 2, 3, and 4 months of age.	

Primary: Percentage of Subjects with Seroprotection Against Poliovirus 1, 2, and 3 Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Percentage of Subjects with Seroprotection Against Poliovirus 1, 2, and 3 Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine
End point description:	
Anti-Poliovirus types 1, 2, 3 neutralizing antibody titers were measured using microneutralization assay. Seroprotection was defined as Anti-Poliovirus types 1, 2, and 3 antibody titers ≥8 (1/dil).	
End point type	Primary
End point timeframe:	
1 month post-primary vaccination series	

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	152	148	
Units: Percentage of subjects				
number (not applicable)				
Anti-Poliovirus 1	100	100	100	
Anti-Poliovirus 2	100	100	100	
Anti-Poliovirus 3	99.33	100	100	

Statistical analyses

Statistical analysis title	Non-inferiority;Anti-Polio 1; Sequential 1-Control

Statistical analysis description:

Non-inferiority analysis of IPV-OPV-OPV (Sequential 1) over the OPV-OPV-OPV (control) for Anti-Poliovirus 1 was assessed.

Comparison groups	IPV-OPV-OPV (Sequential 1) v OPV-OPV-OPV (Control)
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Sequential 1 - Control
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	2.53

Notes:

[1] - Non-inferiority was demonstrated if the lower limit of the two-sided 95% confidence interval of the observed difference was greater than -10% for each serotype and each comparison. IPV-OPV-OPV was non-inferior to OPV-OPV-OPV.

Statistical analysis title	Non-inferiority;Anti-Polio 2; Sequential 1-Control

Statistical analysis description:

Non-inferiority analysis of IPV-OPV-OPV (Sequential 1) over the OPV-OPV-OPV (control) for Anti-Poliovirus 2 was assessed.

Comparison groups	IPV-OPV-OPV (Sequential 1) v OPV-OPV-OPV (Control)
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Sequential 1 - Control
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	2.53

Notes:

[2] - Non-inferiority was demonstrated if the lower limit of the two-sided 95% confidence interval of the observed difference was greater than -10% for each serotype and each comparison. IPV-OPV-OPV was non-inferior to OPV-OPV-OPV.

Statistical analysis title	Non-inferiority;Anti-Polio 3; Sequential 1-Control

Statistical analysis description:

Non-inferiority analysis of IPV-OPV-OPV (Sequential 1) over the OPV-OPV-OPV (control) for Anti-Poliovirus 3 was assessed.

Comparison groups	IPV-OPV-OPV (Sequential 1) v OPV-OPV-OPV (Control)
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Sequential 1 - Control
Point estimate	-0.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.68
upper limit	1.92

Notes:

[3] - Non-inferiority was demonstrated if the lower limit of the two-sided 95% confidence interval of the observed difference was greater than -10% for each serotype and each comparison. IPV-OPV-OPV was non-inferior to OPV-OPV-OPV.

Statistical analysis title	Non-inferiority;Anti-Polio 1; Sequential 2-Control

Statistical analysis description:

Non-inferiority analysis of IPV-IPV-OPV (Sequential 2) over the OPV-OPV-OPV (control) for Anti-Poliovirus 1 was assessed.

Comparison groups	IPV-IPV-OPV (Sequential 2) v OPV-OPV-OPV (Control)
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Sequential 2 - Control
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.47
upper limit	2.53

Notes:

[4] - Non-inferiority was demonstrated if the lower limit of the two-sided 95% confidence interval of the observed difference was greater than -10% for each serotype and each comparison. IPV-IPV-OPV was non-inferior to OPV-OPV-OPV.

Statistical analysis title	Non-inferiority;Anti-Polio 2; Sequential 2-Control

Statistical analysis description:

Non-inferiority analysis of IPV-IPV-OPV (Sequential 2) over the OPV-OPV-OPV (control) for Anti-Poliovirus 2 was assessed.

Comparison groups	IPV-IPV-OPV (Sequential 2) v OPV-OPV-OPV (Control)
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Sequential 2 - Control
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.47
upper limit	2.53

Notes:

[5] - Non-inferiority was demonstrated if the lower limit of the two-sided 95% confidence interval of the observed difference was greater than -10% for each serotype and each comparison. IPV-IPV-OPV was non-inferior to OPV-OPV-OPV.

Statistical analysis title	Non-inferiority;Anti-Polio 3; Sequential 2-Control

Statistical analysis description:

Non-inferiority analysis of IPV-IPV-OPV (Sequential 2) over the OPV-OPV-OPV (control) for Anti-Poliovirus 3 was assessed.

Comparison groups	IPV-IPV-OPV (Sequential 2) v OPV-OPV-OPV (Control)

Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Sequential 2 - Control
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.47
upper limit	2.53

Notes:

[6] - Non-inferiority was demonstrated if the lower limit of the two-sided 95% confidence interval of the observed difference was greater than -10% for each serotype and each comparison. IPV-IPV-OPV was non-inferior to OPV-OPV-OPV.

Secondary: Percentage of Subjects with Seroprotection Against Poliovirus 1, 2, and 3 Before and Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Percentage of Subjects with Seroprotection Against Poliovirus 1, 2, and 3 Before and Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

Anti-Poliovirus types 1, 2, 3 neutralizing antibody titers were measured using microneutralization assay. Seroprotection was defined as Anti-Poliovirus types 1, 2, and 3 antibody titers ≥ 8 (1/dil).

End point type	Secondary

End point timeframe:

Pre-Primary and 1 month Post-Primary vaccination series

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	152	148	
Units: Percentage of subjects				
number (not applicable)				
Anti-Poliovirus 1; Pre-Primary	44.7	46.7	43.9	
Anti-Poliovirus 1; Post-Primary	100	100	100	
Anti-Poliovirus 2; Pre-Primary	42	34.2	32.4	
Anti-Poliovirus 2; Post-Primary	100	100	100	
Anti-Poliovirus 3; Pre-Primary	28	23	21.6	
Anti-Poliovirus 3; Post-Primary	99.3	100	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Anti-Polio 1, 2, and 3 Antibodies Before and Following A Sequential Three-Dose Primary Vaccination Series With Inactivated

Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Geometric Mean Titers of Anti-Polio 1, 2, and 3 Antibodies Before and Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

Anti-Poliovirus types 1, 2, 3 neutralizing antibody titers were measured using microneutralization assay.

End point type	Secondary

End point timeframe:

Pre-Primary and 1 month Post-Primary vaccination series

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	152	148	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Poliovirus 1; Pre-Primary	8.45 (7.11 to 10)	9.08 (7.62 to 10.8)	8.67 (7.27 to 10.3)	
Anti-Poliovirus 1; Post-Primary	2101 (1715 to 2573)	1542 (1251 to 1900)	2764 (2299 to 3324)	
Anti-Poliovirus 2; Pre-Primary	7.87 (6.75 to 9.18)	6.92 (6 to 7.98)	6.59 (5.74 to 7.57)	
Anti-Poliovirus 2; Post-Primary	743 (653 to 844)	2285 (1945 to 2683)	744 (653 to 848)	
Anti-Poliovirus 3; Pre-Primary	6.17 (5.39 to 7.07)	5.6 (4.99 to 6.27)	5.6 (4.91 to 6.38)	
Anti-Poliovirus 3; Post-Primary	1473 (1235 to 1755)	1854 (1442 to 2384)	671 (563 to 799)	

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer Ratios of Anti-Polio 1, 2, and 3 Antibodies Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Geometric Mean Titer Ratios of Anti-Polio 1, 2, and 3 Antibodies Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

Anti-Poliovirus types 1, 2, 3 neutralizing antibody titers were measured using microneutralization assay.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 30 post-primary vaccinations.

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	152	148	
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Poliovirus 1	249 (188 to 328)	170 (128 to 224)	319 (252 to 403)	
Anti-Poliovirus 2	94.3 (75.8 to 117)	330 (259 to 421)	113 (93.6 to 136)	
Anti-Poliovirus 3	239 (192 to 296)	331 (248 to 442)	120 (96.6 to 148)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Seroprotection Against Poliovirus 1, 2, and 3 Fourteen Months After A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Percentage of Subjects with Seroprotection Against Poliovirus 1, 2, and 3 Fourteen Months After A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

Anti-Poliovirus types 1, 2, 3 neutralizing antibody titers were measured using microneutralization assay. Seroprotection was defined as Anti-Poliovirus types 1, 2, and 3 antibody titers ≥ 8 (1/dil).

End point type	Secondary

End point timeframe:

14 months post-dose 3 of primary vaccination series

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	148	150	149	
Units: Percentage of subjects				
number (not applicable)				
Anti-Poliovirus 1	100	99.3	100	
Anti-Poliovirus 2	100	100	100	
Anti-Poliovirus 3	98	96.7	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Each and Any Three-Dose Primary Series Vaccination with Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine.

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Each and Any Three-Dose Primary Series Vaccination with Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine.

End point description:

Solicited injection-site reactions, Tenderness, Erythema and Swelling, Systemic reactions, Fever (Temperature), Vomiting, Abnormal crying, Drowsiness, Loss of appetite and Irritability. Grade 3 Tenderness, cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling ≥ 50 mm;
Fever, > 39°C (axillary); Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Abnormal crying, > 3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Loss of appetite, refuses ≥ 3 feeds/meals or refuses most feeds/meals; and Irritability, inconsolable.

End point type	Secondary

End point timeframe:

Day 0 up to 14 months post-vaccination

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152	152	152	
Units: Percentage of Subjects				
number (not applicable)				
Injection-site Tenderness (Post-any injection)	18.4	21.1	0	
Grade 3 Injection-site Tenderness (post-any inj.)	0	0	0	
Injection-site Tenderness (Post-injection 1)	18.4	15.1	0	
Grade 3 Injection-site Tenderness (Post-inj. 1)	0	0	0	
Injection-site Tenderness (Post-injection 2)	0	13.8	0	
Grade 3 Injection-site Tenderness (Post-inj. 2)	0	0	0	
Injection-site Erythema (Post-any injection)	7.9	7.2	0	
Grade 3 Injection-site Erythema (Post-any inj.)	1.3	0	0	
Injection-site Erythema (Post-injection 1)	7.9	3.9	0	
Grade 3 Injection-site Erythema (Post-inj. 1)	1.3	0	0	
Injection-site Erythema (Post-injection 2)	0	3.9	0	
Grade 3 Injection-site Erythema (Post-inj. 2)	0	0	0	
Injection-site Swelling (Post-any injection)	3.9	0.7	0	

Grade 3 Injection-site Swelling (Post-any inj)	0	0	0	
Injection-site Swelling (Post-injection 1)	3.9	0.7	0	
Grade 3 Injection-site Swelling (Post-inj. 1)	0	0	0	
Injection-site Swelling (Post-injection 2)	0	0.7	0	
Grade 3 Injection-site Swelling (Post-inj. 2)	0	0	0	
Fever (Post-any injection)	28.3	29.6	24.3	
Grade 3 Fever (Post-any injection)	1.3	0	0.7	
Fever (Post-injection 1)	6.6	10.5	7.9	
Grade 3 Fever (Post-injection 1)	0.7	0	0	
Fever (Post-injection 2)	11.2	10.5	7.2	
Grade 3 Fever (Post-injection 2)	0	0	0	
Fever (Post-iinjection 3)	14.5	13.2	14.6	
Grade 3 Fever (Post-injection 3)	0.7	0	0.7	
Vomiting (Post-any injection)	44.7	36.8	44.1	
Grade 3 Vomiting (Post-any injection)	0.7	2	2.6	
Vomiting (Post-injection 1)	33.6	27.6	33.6	
Grade 3 Vomiting (Post-injection 1)	0.7	0.7	1.3	
Vomiting (Post-injection 2)	17.8	21.1	18.4	
Grade 3 Vomiting (Post-injection 2)	0	0.7	1.3	
Vomiting (Post-injection 3)	11.8	10.5	13.9	
Grade 3 Vomiting (Post-injection 3)	0	0.7	0	
Abnormal crying (Post-any injection)	51.3	50.7	43.4	
Grade 3 Abnormal crying (Post-any injection)	2.6	2	5.9	
Abnormal crying (Post-injection 1)	37.5	33.6	30.3	
Grade 3 Abnormal crying (Post-injection 1)	2.6	1.3	3.9	
Abnormal crying (Post-injection 2)	23	32.9	18.9	
Grade 3 Abnormal crying (Post-injection 2)	0.7	0.7	1.3	
Abnormal crying (Post-injection 3)	16.4	8.6	16.6	
Grade 3 Abnormal crying (Post-injection 3)	0	0	0.7	
Drowsiness (Post-any injection)	32.9	30.9	28.9	
Grade 3 Drowsiness (Post-any injection)	0.7	1.3	1.3	
Drowsiness (Post-injection 1)	21.1	23	19.1	
Grade 3 Drowsiness (Post-injection 1)	0.7	1.3	1.3	
Drowsiness (Post-injection 2)	13.8	13.8	11.8	
Grade 3 Drowsiness (Post-injection 2)	0	0	0	
Drowsiness (Post-injection 3)	10.5	5.9	9.3	
Grade 3 Drowsiness (Post-injection 3)	0	0	0	
Appetite Loss (Post-any injection)	32.9	34.9	28.9	
Grade 3 Appetite Loss (Post-any injection)	2.6	0	0.7	
Appetite Loss (Post-injection 1)	21.1	28.3	17.1	
Grade 3 Appetite Loss (Post-injection 1)	1.3	0	0.7	
Appetite Loss (Post-injection 2)	7.9	13.2	12.5	
Grade 3 Appetite Loss (Post-injection 2)	0.7	0	0	
Appetite Loss (Post-injection 3)	13.2	9.2	8.6	
Grade 3 Appetite Loss (Post-injection 3)	0.7	0	0	
Irritability (Post-any injection)	32.2	32.2	25.7	

Grade 3 Irritability (Post-any injection)	2	0.7	3.3	
Irritability (Post-injection 1)	24.3	21.7	17.8	
Grade 3 Irritability (Post-injection 1)	1.3	0	2	
Irritability (Post-injection 2)	12.5	15.1	11.8	
Grade 3 Irritability (Post-injection 2)	0.7	0.7	0.7	
Irritability (Post-injection 3)	10.5	5.9	9.9	
Grade 3 Irritability (Post-injection 3)	0	0	1.3	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers of Anti-Polio 1, 2, and 3 Antibodies Fourteen (14) Months Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Geometric Mean Titers of Anti-Polio 1, 2, and 3 Antibodies Fourteen (14) Months Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

Anti-Poliovirus types 1, 2, 3 neutralizing antibody titers were measured using microneutralization assay.

End point type	Other pre-specified

End point timeframe:

14 months post-dose 3 of primary vaccination series

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	148	150	149	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Poliovirus 1	581 (467 to 723)	342 (270 to 433)	977 (789 to 1209)	
Anti-Poliovirus 2	299 (253 to 354)	361 (306 to 427)	262 (223 to 309)	
Anti-Poliovirus 3	242 (196 to 298)	271 (205 to 357)	177 (148 to 211)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Seroprotection Against Poliovirus 1, 2, and 3 Before and Following A Sequential Three-Dose Primary Vaccination

Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Percentage of Subjects with Seroprotection Against Poliovirus 1, 2, and 3 Before and Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

Anti-Poliovirus types 1, 2, 3 neutralizing antibody titers were measured using microneutralization assay. Seroprotection was defined as Anti-Poliovirus types 1, 2, and 3 antibody titers ≥ 8 (1/dil).

End point type	Other pre-specified

End point timeframe:

Pre-Primary, Post-Primary vaccination series

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	152	148	
Units: Percentage of subjects				
number (not applicable)				
Anti-Poliovirus 1; Pre-Primary	18.4	18.7	17	
Anti-Poliovirus 1; Post-Primary	100	99.3	100	
Anti-Poliovirus 2; Pre-Primary	38.3	24.8	20	
Anti-Poliovirus 2; Post-Primary	100	100	100	
Anti-Poliovirus 3; Pre-Primary	20.9	13.6	15.9	
Anti-Poliovirus 3; Post-Primary	100	100	99.3	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers of Anti-Polio 1, 2, and 3 Antibodies Before and Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Geometric Mean Titers of Anti-Polio 1, 2, and 3 Antibodies Before and Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

Anti-Poliovirus types 1, 2, 3 neutralizing antibody titers were measured using microneutralization assay.

End point type	Other pre-specified

End point timeframe:

Pre-Primary and Post-Primary vaccination series

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	152	148	
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Poliovirus 1; Pre-Primary	3.37 (2.92 to 3.88)	3.42 (2.95 to 3.97)	3.26 (2.81 to 3.78)	
Anti-Poliovirus 1; Post-Primary	1829 (1467 to 2280)	2572 (2043 to 3239)	442 (358 to 545)	
Anti-Poliovirus 2; Pre-Primary	5.17 (4.37 to 6.11)	4.11 (3.48 to 4.85)	3.65 (3.16 to 4.21)	
Anti-Poliovirus 2; Post-Primary	2190 (1914 to 2506)	8229 (7152 to 9469)	890 (763 to 1038)	
Anti-Poliovirus 3; Pre-Primary	3.58 (3.13 to 4.09)	3.22 (2.87 to 3.6)	3.21 (2.82 to 3.66)	
Anti-Poliovirus 3; Post-Primary	1409 (1171 to 1694)	2053 (1580 to 2666)	335 (277 to 406)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titer Ratios of Anti-Polio 1, 2, and 3 Antibodies Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Geometric Mean Titer Ratios of Anti-Polio 1, 2, and 3 Antibodies Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

Anti-Poliovirus types 1, 2, 3 neutralizing antibody titers were measured using microneutralization assay.

End point type	Other pre-specified

End point timeframe:

Day 0 (pre-vaccination) and Day 30 Post-Primary vaccinations

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	149	150	147	
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Poliovirus 1	557 (421 to 737)	746 (557 to 998)	134 (105 to 171)	
Anti-Poliovirus 2	431 (338 to 549)	2022 (1583 to 2583)	244 (197 to 303)	
Anti-Poliovirus 3	396 (318 to 494)	637 (476 to 852)	107 (85.7 to 135)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Seroprotection Against Poliovirus 1, 2 and 3 Fourteen Months After A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Percentage of Subjects with Seroprotection Against Poliovirus 1, 2 and 3 Fourteen Months After A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

Seroprotection was defined as post-vaccination antibody titers 1 ≥8 1/dil.

End point type	Other pre-specified

End point timeframe:

Fourteen Months Post-Primary Vaccination Series

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	148	150	149	
Units: Percentage of Subjects				
number (not applicable)				
Anti-Polio 1 Antibody	100	99.3	96.6	
Anti-Polio 2 Antibody	100	100	100	
Anti-Polio 3 Antibody	98	98	99.3	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers of Anti-polio 1, 2 and 3 Antibodies Fourteen Months Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point title	Geometric Mean Titers of Anti-polio 1, 2 and 3 Antibodies Fourteen Months Following A Sequential Three-Dose Primary Vaccination Series With Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) and Commercially Available Oral Poliomyelitis Vaccine

End point description:

End point type	Other pre-specified

End point timeframe:

Fourteen months post-primary series vaccination

End point values	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	148	150	149	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1	330 (267 to 407)	390 (316 to 481)	123 (98.7 to 153)	
Anti-Polio 2	669 (562 to 795)	1072 (897 to 1282)	349 (291 to 418)	
Anti-Polio 3	154 (126 to 189)	199 (155 to 256)	86.6 (72.7 to 103)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse event were reported from Day 0 up to 16 months post-vaccination.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups	
Reporting group title	IPV-OPV-OPV (Sequential 1)
Reporting group description:	
Infants ≥ 2 months and under 3 months of age sequentially received Sanofi Pasteur's injectable Inactivated Poliovirus Vaccine (IPV; IMOVAX Polio™) at 2 months and commercially available Oral Poliovirus Vaccine (OPV) at 3 and 4 months of age.	
Reporting group title	IPV-IPV-OPV (Sequential 2)
Reporting group description:	
Infants ≥ 2 months and under 3 months of age sequentially received Sanofi Pasteur's injectable Inactivated Poliovirus Vaccine (IPV; IMOVAX Polio™) at 2 and 3 months and commercially available Oral Poliovirus Vaccine (OPV) at 4 months of age.	
Reporting group title	OPV-OPV-OPV (Control)
Reporting group description:	
Infants ≥ 2 months and under 3 months of age sequentially received commercially available Oral Poliovirus Vaccine (OPV) at 2, 3, and 4 months of age.	

Serious adverse events	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 152 (3.29%)	7 / 152 (4.61%)	9 / 152 (5.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Tachycardia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial damage			
subjects affected / exposed	0 / 152 (0.00%)	2 / 152 (1.32%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			

subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Infantile diarrhea			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hirschsprung’s disease			
subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Asthmatic bronchopneumonia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthmatic bronchitis			
subjects affected / exposed	1 / 152 (0.66%)	0 / 152 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	3 / 152 (1.97%)	1 / 152 (0.66%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	1 / 152 (0.66%)	3 / 152 (1.97%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial pneumonia			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	3 / 152 (1.97%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Severe pneumonia			

subjects affected / exposed	0 / 152 (0.00%)	0 / 152 (0.00%)	1 / 152 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral enteritis			
subjects affected / exposed	0 / 152 (0.00%)	1 / 152 (0.66%)	0 / 152 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	IPV-OPV-OPV (Sequential 1)	IPV-IPV-OPV (Sequential 2)	OPV-OPV-OPV (Control)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 152 (51.32%)	77 / 152 (50.66%)	67 / 152 (44.08%)
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	50 / 152 (32.89%)	47 / 152 (30.92%)	44 / 152 (28.95%)
occurrences (all)	50	47	44
General disorders and administration site conditions			
Injection site tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	28 / 152 (18.42%)	32 / 152 (21.05%)	0 / 152 (0.00%)
occurrences (all)	28	32	0
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 152 (7.89%)	11 / 152 (7.24%)	0 / 152 (0.00%)
occurrences (all)	12	11	0
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	43 / 152 (28.29%)	45 / 152 (29.61%)	37 / 152 (24.34%)
occurrences (all)	43	45	37
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			

subjects affected / exposed	68 / 152 (44.74%)	56 / 152 (36.84%)	67 / 152 (44.08%)
occurrences (all)	68	56	67
Psychiatric disorders			
Abnormal crying			
alternative assessment type: Systematic			
subjects affected / exposed	78 / 152 (51.32%)	77 / 152 (50.66%)	66 / 152 (43.42%)
occurrences (all)	78	77	66
Irritability			
subjects affected / exposed	49 / 152 (32.24%)	49 / 152 (32.24%)	39 / 152 (25.66%)
occurrences (all)	49	49	39
Metabolism and nutrition disorders			
Appetite loss			
alternative assessment type: Systematic			
subjects affected / exposed	50 / 152 (32.89%)	53 / 152 (34.87%)	44 / 152 (28.95%)
occurrences (all)	50	53	44

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2012	The Sponsor's Responsible Medical Officer was changed; The age range for Visit 05 was clarified to 'between 18 and <19 months of age'; and an observational objective was added to the protocol in order to obtain the immunogenicity results from Global Clinical Immunology (GCI) Sanofi Pasteur, Swiftwater, PA. USA, in addition to the results from National Institute for Food and Drug Control (NIFDC), China.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported