Clinical trial results:
Immunogenicity and Safety of IMOVAX POLIO® Subcutaneous as a Booster Given in Pre-school Age Children in Japan (IPV46)

Summary

EudraCT number	2015-003279-31
Trial protocol	Outside EU/EEA
Global end of trial date	03 June 2014

Results information

Result version number	v1 (current)
This version publication date	12 May 2016
First version publication date	12 May 2016

Trial information

Trial identification

Sponsor protocol code	IPV46/EFC13614

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02005536
WHO universal trial number (UTN)	U1111-1143-8561

Notes:

Sponsors

Sponsor organisation name	Sanofi K.K.
Sponsor organisation address	3-20-2, Nishi Shinjuku, Shinjuku-ku, Tokyo, Japan, 163-1488
Public contact	PMS Management Supervisor, Sanofi K.K., 33 4376 56799, Emmanuel.vidor@sanofipasteur.com
Scientific contact	PMS Management Supervisor, Sanofi K.K., 33 4376 56799, 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	03 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the booster vaccine response rate against poliovirus types 1, 2 and 3 one month following the vaccination dose with SP059 as a second booster.

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	02 December 2013
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	Japan: 60
Worldwide total number of subjects	60
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	60
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:

Subjects were enrolled from 02 December 2013 to 28 April 2014 at 4 clinic centers in Japan.

Pre-assignment

Screening details:

A total of 60 subjects who met all of the inclusion and none of the exclusion criteria were enrolled and vaccinated. A subject with an exclusion criteria was later discovered and was excluded in the per-protocol analysis set.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Arm title	IMOVAX POLIO® Vaccine Group

Arm description:

Subjects received a single booster dose of IMOVAX POLIO® vaccine on Day 0.

Arm type	Experimental
Investigational medicinal product name	SP059, IMOVAX POLIO® (Inactivated Poliovirus Vaccine; IPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous, single dose.

Number of subjects in period 1	IMOVAX POLIO® Vaccine Group
Started	60
Completed	60

Baseline characteristics

Reporting groups	
Reporting group title	IMOVAX POLIO® Vaccine Group
Reporting group description:	
Subjects received a single booster dose of IMOVAX POLIO® vaccine on Day 0.	

Reporting group values	IMOVAX POLIO® Vaccine Group	Total	
Number of subjects	60	60	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	60	60	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	4		
standard deviation	± 0.2	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	35	35	

End points

End points reporting groups

Reporting group title	IMOVAX POLIO® Vaccine Group
Reporting group description:	
Subjects received a single booster dose of IMOVAX POLIO® vaccine on Day 0.	

Primary: Percentage of Participants With Booster Responses Against Polio Antigens Following Vaccination With IMOVAX POLIO®

End point title	Percentage of Participants With Booster Responses Against Polio Antigens Following Vaccination With IMOVAX POLIO®[1]
End point description:	
A booster response was defined as a 4-fold increase from pre-booster to post-booster vaccination. Anti-polio virus antibodies were assessed by virus neutralization assay.	
End point type	Primary
End point timeframe:	
Day 28 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: Descriptive analyses were performed based on the study group and the study vaccine administered for this outcome.

End point values	IMOVAX POLIO® Vaccine Group			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: Percentage of subjects				
number (not applicable)				
Anti-Polio 1	78			
Anti-Polio 2	78			
Anti-Polio 3	79.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Vaccine Antigens Before and After Vacination With IMOVAX POLIO®

End point title	Geometric Mean Titers of Vaccine Antigens Before and After Vacination With IMOVAX POLIO®
End point description:	
Anti-polio virus antibodies were assessed by virus neutralization assay.	
End point type	Secondary
End point timeframe:	
Day 0 (pre-booster vaccination) and Day 28 post-booster vaccination	

End point values	IMOVAX POLIO® Vaccine Group			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Polio 1 (pre-vaccination)	312.6 (241.8 to 404.1)			
Anti-Polio 1 (post-vaccination)	3794.9 (3011.5 to 4782.1)			
Anti-Polio 2 (pre-vaccination)	795.4 (591.8 to 1069.1)			
Anti-Polio 2 (post-vaccination)	9213.2 (6754.5 to 12567)			
Anti-Polio 3 (pre-vaccination)	314.5 (219.5 to 450.4)			
Anti-Polio 3 (post-vaccination)	5242.1 (3912.9 to 7022.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Seroprotection Against Polio Antigens Before and After Booster Vaccination With IMOVAX POLIO®

End point title	Percentage of Participants With Seroprotection Against Polio Antigens Before and After Booster Vaccination With IMOVAX POLIO®

End point description:

Seroprotection was defined as a titer of ≥ 8 (1/dil) pre-booster or post-booster vaccination. Anti-polio virus antibodies were assessed by virus neutralization assay.

End point type	Secondary

End point timeframe:

Day 0 (pre-booster vaccination) and Day 28 post-booster vaccination

End point values	IMOVAX POLIO® Vaccine Group			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: Percentage of subjects				
number (not applicable)				
Anti-Polio 1 (pre-vaccination)	100			

Anti-Polio 1 (post-vaccination)	100			
Anti-Polio 2 (pre-vaccination)	100			
Anti-Polio 2 (post-vaccination)	100			
Anti-Polio 3 (pre-vaccination)	98.3			
Anti-Polio 3 (post-vaccination)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean of Individual Titer Ratios of Vaccine Antigens Following Booster Vacination With IMOVAX POLIO®

End point title	Geometric Mean of Individual Titer Ratios of Vaccine Antigens Following Booster Vacination With IMOVAX POLIO®

End point description:

Anti-polio virus anti-bodies were assessed by virus neutralization assay. The geometric mean titer ratio is the post-booster to pre-booster geometric mean ratio values.

End point type	Secondary

End point timeframe:

Day 28 post-booster vaccination

End point values	IMOVAX POLIO® Vaccine Group			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: Titer ratios (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Polio 1	12.1 (8.5 to 17.4)			
Anti-Polio 2	11.6 (7.7 to 17.5)			
Anti-Polio 3	16.7 (9.8 to 28.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Reporting a Solicited Injection Site or Systemic Reaction Following Booster Vaccination With IMOVAX POLIO®

End point title	Number of Participants Reporting a Solicited Injection Site or Systemic Reaction Following Booster Vaccination With IMOVAX POLIO®

End point description:

Solicited Injection Site Reactions: Pain, Erythema, Swelling. Solicited Systemic Reactions: Fever, Headache, Malaise, Myalgia. Grade 3 was defined as incapacitating, unable to perform usual activities

for Pain; diameter ≥ 50 mm for Erythema and Swelling; Temperature ≥ 39.0°C for Fever; and significant, prevents daily activity for Headache, Malaise, and Myalgia.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-vaccination

End point values	IMOVAX POLIO® Vaccine Group			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Number of subjects				
number (not applicable)				
Any Injection site Pain	13			
Grade 3 Injection site Pain	0			
Any Injection site Erythema	41			
Grade 3 Injection site Erythema	1			
Any Injection site Swelling	21			
Grade 3 Injection site Swelling	0			
Any Fever	8			
Grade 3 Fever	2			
Any Headache	4			
Grade 3 Headache	0			
Any Malaise	18			
Grade 3 Malaise	0			
Any Myalgia	1			
Grade 3 Myalgia	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 (post-booster vaccination) up to Day 28 post-booster vaccination.

Adverse event reporting additional description:

The total number (47) reporting other adverse events at the 5% frequency are those subjects with solicited injection site and systemic reactions.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	IMOVAX POLIO® Vaccine Group

Reporting group description:

Subjects received a single booster dose of IMOVAX POLIO® vaccine on Day 0.

Serious adverse events	IMOVAX POLIO® Vaccine Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	IMOVAX POLIO® Vaccine Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 60 (78.33%)		
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
General disorders and administration site conditions			
Fever			
alternative assessment type: Systematic			

subjects affected / exposed	8 / 60 (13.33%)		
occurrences (all)	8		
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	41 / 60 (68.33%)		
occurrences (all)	41		
Injection site Pain			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 60 (21.67%)		
occurrences (all)	13		
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 60 (35.00%)		
occurrences (all)	21		
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 60 (30.00%)		
occurrences (all)	18		
Pyrexia			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	11		
Upper respiratory tract infection			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Varicella			

subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 September 2013	Minor logistic modifications.
25 September 2013	Minor logistic modifications

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported