Clinical trial results:
Immunogenicity and Safety of Fractional Doses of Sanofi Pasteur's Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) Administered Intradermally versus Full Doses of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) Administered Intramuscularly in Healthy Infants in The Philippines

Summary

EudraCT number	2015-005183-42
Trial protocol	Outside EU/EEA
Global end of trial date	18 July 2008

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	IPV25

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00604058
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 37 70 26, RegistryContactUS@sanofipasteur.com
Scientific contact	Franchise Medical Director, Sanofi Pasteur SA, 33 4 37 37 70 26, RegistryContactUS@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	04 December 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the non-inferiority of fractional doses of IPV administered intradermally versus full doses of IPV administered intramuscularly, in terms of seroprotection rates (polio types 1, 2 and 3) one month after the three-dose primary vaccination.

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	19 February 2008
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: 236
Worldwide total number of subjects	236
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)	236
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:

The study subjects were enrolled from 19 February 2008 to 08 March 2008 at 1 clinic center in the Philippines.

Pre-assignment

Screening details:

A total of 236 subjects who met all inclusion and none of the exclusion criteria were randomized 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	Group A; Fractional Dose of IMOVAX Polio™

Arm description:

Infants received fractional doses (0.1 mL or 1/5 of a dose) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally at 6, 10, and 14 weeks 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, 1 dose each at 6, 10, and 14 weeks of age.

Arm title	Group B; Full Dose of IMOVAX Polio™

Arm description:

Infants received full doses (0.5 mL) of IPV intramuscularly at 6, 10, and 14 weeks 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, intramuscular into the anterolateral area of the right thigh, 1 dose each at 6, 10, and 14 weeks of age.

Number of subjects in period 1	Group A; Fractional Dose of IMOVAX Polio™	Group B; Full Dose of IMOVAX Polio™
Started	118	118
Completed	115	115
Not completed	3	3
Consent withdrawn by subject	2	3
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Group A; Fractional Dose of IMOVAX Polio™
Reporting group description:	
Infants received fractional doses (0.1 mL or 1/5 of a dose) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally at 6, 10, and 14 weeks of age.	
Reporting group title	Group B; Full Dose of IMOVAX Polio™
Reporting group description:	
Infants received full doses (0.5 mL) of IPV intramuscularly at 6, 10, and 14 weeks of age.	

Reporting group values	Group A; Fractional Dose of IMOVAX Polio™	Group B; Full Dose of IMOVAX Polio™	Total
Number of subjects	118	118	236
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)	118	118	236
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: days			
arithmetic mean	45.5	45.5	
standard deviation	± 2.1	± 2.2	-
Gender categorical Units: Subjects			
Female	59	74	133
Male	59	44	103

End points

End points reporting groups

Reporting group title	Group A; Fractional Dose of IMOVAX Polio™
Reporting group description:	
Infants received fractional doses (0.1 mL or 1/5 of a dose) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally at 6, 10, and 14 weeks of age.	
Reporting group title	Group B; Full Dose of IMOVAX Polio™
Reporting group description:	
Infants received full doses (0.5 mL) of IPV intramuscularly at 6, 10, and 14 weeks of age.	

Primary: Percentage of Infant Subjects with Seroprotection Against Poliovirus 1, 2 and 3 Following A Three-Dose Primary Vaccination Series with Either Fractional Doses Or Full Doses of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)

End point title	Percentage of Infant Subjects with Seroprotection Against Poliovirus 1, 2 and 3 Following A Three-Dose Primary Vaccination Series with Either Fractional Doses Or Full Doses of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)
End point description:	
Anti-poliovirus types 1, 2, and 3 titers were measured by neutralization assay. Seroprotection was defined as Anti-poliovirus types 1, 2, 3 titers ≥ 8 (1/dil).	
End point type	Primary
End point timeframe:	
1 month post-dose 3 of primary vaccination	

End point values	Group A; Fractional Dose of IMOVAX Polio™	Group B; Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	114		
Units: Percentage of subjects				
number (not applicable)				
Anti-Polio 1	100	100		
Anti-Polio 2	100	100		
Anti-Polio 3	99.1	100		

Statistical analyses

Statistical analysis title	Anti-Polio 1; Group A-Group B
Statistical analysis description:	
Non-inferiority analysis of fractional doses of IPV administered intradermally versus full doses of IPV administered intramuscularly, in terms of seroprotection rates one month after the three-dose primary vaccination administered at 6, 10, and 14 weeks of age.	
Comparison groups	Group B; Full Dose of IMOVAX Polio™ v Group A; Fractional Dose of IMOVAX Polio™

Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Group A-Group B
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.26

Notes:

[1] - For each polio type, the non-inferiority is demonstrated if the 95% confidence interval of the difference lies entirely above -5%. Group A was non-inferior to Group B.

Statistical analysis title	Anti-Polio 2; Group A-Group B

Statistical analysis description:

Non-inferiority analysis of fractional doses of IPV administered intradermally versus full doses of IPV administered intramuscularly, in terms of seroprotection rates one month after the three-dose primary vaccination administered at 6, 10, and 14 weeks of age.

Comparison groups	Group A; Fractional Dose of IMOVAX Polio™ v Group B; Full Dose of IMOVAX Polio™
Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Group A-Group B
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.26

Notes:

[2] - For each polio type, the non-inferiority is demonstrated if the 95% confidence interval of the difference lies entirely above -5%. Group A was non-inferior to Group B.

Statistical analysis title	Anti-Polio 3; Group A-Group B

Statistical analysis description:

Non-inferiority analysis of fractional doses of IPV administered intradermally versus full doses of IPV administered intramuscularly, in terms of seroprotection rates one month after the three-dose primary vaccination administered at 6, 10, and 14 weeks of age.

Comparison groups	Group A; Fractional Dose of IMOVAX Polio™ v Group B; Full Dose of IMOVAX Polio™
Number of subjects included in analysis	223
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Group A-Group B
Point estimate	-0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.01
upper limit	2.43

Notes:

[3] - For each polio type, the non-inferiority is demonstrated if the 95% confidence interval of the difference lies entirely above -5%. For Anti-Polio 3, the lower limit of -5.01% was equal to the clinically acceptable limit for non-inferiority (-5%).

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Pre-Primary, Adjusted Pre-Primary, and Post-Primary vaccination

End point values	Group A; Fractional Dose of IMOVAX Polio™	Group B; Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	114		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Polio 1; Pre-Primary	10.4 (8 to 13.4)	11.7 (8.9 to 15.4)		
Anti-Polio 1; Adjusted Pre-Primary	1.2 (0.9 to 1.5)	1.3 (1 to 1.7)		
Anti-Polio 1; Post-Primary	221.2 (188.8 to 259.1)	585.3 (482.1 to 710.5)		
Anti-Polio 2; Pre-Primary	16.5 (12.9 to 21.1)	16.7 (12.8 to 21.6)		
Anti-Polio 2; Adjusted Pre-Primary	1.9 (1.5 to 2.4)	1.9 (1.4 to 2.4)		
Anti-Polio 2; Post-Primary	234.2 (186.4 to 294.2)	795.6 (638.1 to 992.1)		
Anti-Polio 3; Pre-Primary	7.8 (6 to 10)	6.7 (5.2 to 8.6)		
Anti-Polio 3; Adjusted Pre-Primary	0.9 (0.7 to 1.1)	0.7 (0.6 to 1)		
Anti-Polio 3; Post-Primary	194.7 (157.7 to 240.4)	774.2 (622.2 to 963.3)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Geometric Mean Titer Ratios of Anti-polio 1, 2, and 3 Antibodies Following A Three-Dose Primary Vaccination series with Either Fractional Doses Or Full Doses of Inactivated

	Poliomyelitis Vaccine (IMOVAX Polio™)

End point description:

Anti-poliovirus types 1, 2, and 3 titers were measured by neutralization assay. Geometric mean titer ratios were based on Post/Pre-Primary vaccination ≥ 4-fold increase. Individual adjusted ratios were calculated with individual titers adjusted according to the level of maternal anti-Polio antibodies in subjects' serum at V01 and their estimated levels that would have been observed at V04 if vaccination had not been performed.

End point type	Secondary

End point timeframe:

Post/Pre-Primary

End point values	Group A; Fractional Dose of IMOVAX Polio™	Group B; Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	114		
Units: Titer ratio (1/dil)				
geometric mean (confidence interval 95%)				
Anti-Polio 1; Individual ratio	21.3 (15.8 to 28.8)	49.8 (34.6 to 71.8)		
Anti-Polio 2; Individual ratio	14.2 (9.5 to 21.2)	47.8 (31.9 to 71.6)		
Anti-Polio 3; Individual ratio	25 (17.6 to 35.6)	115.7 (80.6 to 166)		
Anti-Polio 1; Individual adjusted ratio	188.3 (139.1 to 254.9)	446.3 (310.1 to 642.4)		
Anti-Polio 2; Individual adjusted ratio	125.7 (84.4 to 187.2)	427.8 (285.9 to 640.2)		
Anti-Polio 3; Individual adjusted ratio	221.3 (155.1 to 315.7)	1035.9 (724.9 to 1480.3)		

Statistical analyses

No statistical analyses for this end point

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

End point description:

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

End point type	Secondary

End point timeframe:

Pre-Primary, Adjusted Pre-Primary, and Post-Primary vaccination

End point values	Group A; Fractional Dose of IMOVAX Polio™	Group B; Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	114		
Units: Percentage of subjects				
number (not applicable)				
Anti-Polio 1; Pre-Primary; ≥ 4 (1/dil)	74.3	76.3		
Anti-Polio 1; Adjusted Pre-Primary; ≥ 4 (1/dil)	20.2	22.8		
Anti-Polio 1; Post-Primary; ≥ 4 (1/dil)	100	100		
Anti-Polio 1; Pre-Primary; ≥ 8 (1/dil)	59.6	56.1		
Anti-Polio 1; Adjusted Pre-Primary; ≥ 8 (1/dil)	10.1	12.3		
Anti-Polio 1; Post-Primary; ≥ 8 (1/dil)	100	100		
Anti-Polio 2; Pre-Primary; ≥ 4 (1/dil)	89	86.8		
Anti-Polio 2; Adjusted Pre-Primary; ≥ 4 (1/dil)	30.3	33.3		
Anti-Polio 2; Post-Primary; ≥ 4 (1/dil)	100	100		
Anti-Polio 2; Pre-Primary; ≥ 8 (1/dil)	71.6	69.3		
Anti-Polio 2; Adjusted Pre-Primary; ≥ 8 (1/dil)	16.5	15.8		
Anti-Polio 2; Post-Primary; ≥ 8 (1/dil)	100	100		
Anti-Polio 3; Pre-Primary; ≥ 4 (1/dil)	67	58.8		
Anti-Polio 3; Adjusted Pre-Primary; ≥ 4 (1/dil)	13.8	14		
Anti-Polio 3; Post-Primary; ≥ 4 (1/dil)	100	100		
Anti-Polio 3; Pre-Primary; ≥ 8 (1/dil)	45	41.2		
Anti-Polio 3; Adjusted Pre-Primary; ≥ 8 (1/dil)	9.2	8.8		
Anti-Polio 3; Post-Primary; ≥ 8 (1/dil)	99.1	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Infant Subjects with Solicited Injection-site and Systemic Reactions Following Any and Each Primary Series Vaccination with Either Fractional Doses Or Full Doses of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)

End point title	Percentage of Infant Subjects with Solicited Injection-site and Systemic Reactions Following Any and Each Primary Series Vaccination with Either Fractional Doses Or Full Doses of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™)

End point description:

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

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) up to Day 8 post-any and each vaccine injection

End point values	Group A; Fractional Dose of IMOVAX Polio™	Group B; Full Dose of IMOVAX Polio™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	118		
Units: Percentage of subjects				
number (not applicable)				
Injection site Reaction; Post-Any Injection	83.1	59.8		
Injection site Tenderness; Post-Any Injection	60.2	50.4		
Injection site Tenderness; Post-Dose 1	50.8	41		
Injection site Tenderness; Post-Dose 2	35.7	27		
Injection site Tenderness; Post-Dose 3	28.9	18.3		
Injection site Erythema; Post-Any Injection	69.5	29.1		
Injection site Erythema; Post-Dose 1	44.1	12		
Injection site Erythema; Post-Dose 2	48.7	11.3		
Injection site Erythema; Post-Dose 3	39.5	12.2		
Injection site Swelling; Post-Any Injection	21.2	9.4		
Injection site Swelling; Post-Dose 1	11	6.8		
Injection site Swelling; Post-Dose 2	11.3	2.6		
Injection site Swelling; Post-Dose 3	7	3.5		
Solicited systemic reaction; Post-Any Injection	65.3	67.5		
Fever; Post-Any Injection	5.9	10.3		
Fever; Post-Dose 1	4.2	5.1		
Fever; Post-Dose 2	0	2.6		
Fever; Post-Dose 3	1.8	3.5		
Vomiting; Post-Any Injection	15.3	21.4		
Vomiting; Post-Dose 1	12.7	15.4		
Vomiting; Post-Dose 2	2.6	7		
Vomiting; Post-Dose 3	1.8	0		
Crying abnormal; Post-Any Injection	33.9	30.8		
Crying abnormal; Post-Dose 1	23.7	17.9		
Crying abnormal; Post-Dose 2	10.4	13		
Crying abnormal; Post-Dose 3	7.9	5.2		
Drowsiness; Post-Any Injection	37.3	35		
Drowsiness; Post-Dose 1	30.5	27.4		
Drowsiness; Post-Dose 2	8.7	9.6		
Drowsiness; Post-Dose 3	8.8	5.2		
Appetite lost; Post-Any Injection	16.1	19.7		
Appetite lost; Post-Dose 1	12.7	12.8		
Appetite lost; Post-Dose 2	5.2	4.3		
Appetite lost; Post-Dose 3	2.6	4.3		
Irritability; Post-Any Injection	49.2	43.6		
Irritability; Post-Dose 1	43.2	32.5		
Irritability; Post-Dose 2	18.3	13		

Irritability; Post-Dose 3	10.5	9.6		

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 1 month post-dose 3 of the primary vaccination.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Group A; Fractional Dose of IMOVAX Polio™

Reporting group description:

Infants received fractional doses (0.1 mL or 1/5 of a dose) of Inactivated Poliomyelitis Vaccine (IMOVAX Polio™) intradermally at 6, 10, and 14 weeks of age.

Reporting group title	Group B; Full Dose of IMOVAX Polio™

Reporting group description:

Infants received full doses (0.5 mL) of IPV intramuscularly at 6, 10, and 14 weeks of age.

Serious adverse events	Group A; Fractional Dose of IMOVAX Polio™	Group B; Full Dose of IMOVAX Polio™	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 118 (1.69%)	0 / 118 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 118 (1.69%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group A; Fractional Dose of IMOVAX Polio™	Group B; Full Dose of IMOVAX Polio™	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	98 / 118 (83.05%)	79 / 118 (66.95%)	
Nervous system disorders			
Drowsiness; Post-Any Injection			
alternative assessment type: Systematic			

subjects affected / exposed[1]	44 / 118 (37.29%)	41 / 117 (35.04%)	
occurrences (all)	44	41	
General disorders and administration site conditions			
Injection site Tenderness; Post-Any Injection			
alternative assessment type: Systematic			
subjects affected / exposed[2]	71 / 118 (60.17%)	59 / 117 (50.43%)	
occurrences (all)	71	59	
Injection site Erythema; Post-Any Injection			
alternative assessment type: Systematic			
subjects affected / exposed	82 / 118 (69.49%)	34 / 118 (28.81%)	
occurrences (all)	82	34	
Injection site Swelling; Post-Any Injection			
alternative assessment type: Systematic			
subjects affected / exposed[3]	25 / 118 (21.19%)	11 / 117 (9.40%)	
occurrences (all)	25	11	
Fever; Post-Any Injection			
alternative assessment type: Systematic			
subjects affected / exposed[4]	7 / 118 (5.93%)	12 / 117 (10.26%)	
occurrences (all)	7	12	
Pyrexia			
subjects affected / exposed	9 / 118 (7.63%)	8 / 118 (6.78%)	
occurrences (all)	9	8	
Gastrointestinal disorders			
Vomiting; Post-Any Injection			
alternative assessment type: Systematic			
subjects affected / exposed[5]	18 / 118 (15.25%)	25 / 117 (21.37%)	
occurrences (all)	18	25	
Psychiatric disorders			
Crying abnormal; Post-Any Injection			
alternative assessment type: Systematic			
subjects affected / exposed[6]	40 / 118 (33.90%)	36 / 117 (30.77%)	
occurrences (all)	40	36	
Irritability; Post-Any Injection			
alternative assessment type: Systematic			

subjects affected / exposed[7]	58 / 118 (49.15%)	51 / 117 (43.59%)	
occurrences (all)	58	51	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	71 / 118 (60.17%)	77 / 118 (65.25%)	
occurrences (all)	114	122	
Viral infection			
subjects affected / exposed	5 / 118 (4.24%)	8 / 118 (6.78%)	
occurrences (all)	5	9	
Metabolism and nutrition disorders			
Appetite lost; Post-Any Injection			
alternative assessment type: Systematic			
subjects affected / exposed[8]	19 / 118 (16.10%)	23 / 117 (19.66%)	
occurrences (all)	19	23	

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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[6] - 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[7] - 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[8] - 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: This was a solicited adverse event recorded in a diary card within 7 days of vaccination; the total number (N) reflects those subjects for which the diary cards were returned and for which data

were available for the event during the period.

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