Clinical trial results:
Safety of the DTacP-IPV//PRP~T Combined Vaccine (PENTAXIM®) Given as a Three-Dose Primary Vaccination at 2, 3, and 4 Months of Age in Infants in China

Summary

EudraCT number	2015-005404-29
Trial protocol	Outside EU/EEA
Global end of trial date	14 September 2012

Results information

Result version number	v1 (current)
This version publication date	09 June 2016
First version publication date	09 June 2016

Trial information

Trial identification

Sponsor protocol code	E2I60

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01491087
WHO universal trial number (UTN)	U1111-1117-7233

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur, SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon cedex 07, France, F-69367
Public contact	Medical Product Leader, Sanofi Pasteur, SA, 33 4 37 65 67 99, Emmanuel.vidor@sanofipasteur.com
Scientific contact	Medical Product Leader, 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	20 December 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 September 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety after administration of PENTAXIM® at 2, 3, and 4 months of age in the study population.

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 kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were 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 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: 900
Worldwide total number of subjects	900
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)	900
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 02 December 2011 to 14 May 2012 in 3 Chinese provinces/cities.

Pre-assignment

Screening details:

A total of 900 subjects who met the inclusion, but none of the exclusion criteria were enrolled and vaccinated.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Arm title	Study Group

Arm description:

Subjects received DTacP-IPV//PRP~T Combined Vaccine (Pentaxim®) as a three-dose primary vaccination at 2, 3, and 4 Months of Age.

Arm type	Experimental
Investigational medicinal product name	DTacP-IPV//PRP-T combined vaccine
Investigational medicinal product code	
Other name	PENTAXIM™
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, Intramuscular into the anterolateral external aspect of the upper thigh (right or left)

Number of subjects in period 1	Study Group
Started	900
Completed	871
Not completed	29
Consent withdrawn by subject	9
Lost to follow-up	9
Adverse event, non-fatal	9
Serious adverse events	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	900	900	
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)	900	900	
Children (2-11 years)	0	0	
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: months			
arithmetic mean	2.2		
standard deviation	± 0.1	-	
Gender categorical Units: Subjects			
Female	443	443	
Male	457	457	

End points

End points reporting groups

Reporting group title	Study Group
Reporting group description:	
Subjects received DTacP-IPV//PRP~T Combined Vaccine (Pentaxim®) as a three-dose primary vaccination at 2, 3, and 4 Months of Age.	

Primary: Percentage of Infant Subjects with Solicited Injection-site and Systemic Reactions After Any Injection with DTacP-IPV//PRP~T Combined Vaccine (Pentaxim®) Given as a Three-Dose Primary Vaccination.

End point title	Percentage of Infant Subjects with Solicited Injection-site and Systemic Reactions After Any Injection with DTacP-IPV//PRP~T Combined Vaccine (Pentaxim®) Given as a Three-Dose Primary Vaccination.[1]
End point description:	
Solicited injection-site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever (temperature), Vomiting, Crying abnormal, Drowsiness, Appetite Lost, and Irritability. Grade 3 injection-site: Tenderness, Cries when injected limb is moved, or the movement of the injected limb is reduced; Erythema and Swelling > 30 mm. Grade 3: Fever, > 39°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; and Irritability, Inconsolable.	
End point type	Primary
End point timeframe:	
Day 0 up to Day 7 post-any 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 was performed based on the study vaccine administered for this outcome.	

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	900			
Units: Percentage of Subjects				
number (not applicable)				
Injection-site Tenderness	41.3			
Grade 3 injection-site Tenderness	1			
Injection-site Erythema	44.7			
Grade 3 injection-site Erythema	1.4			
Injection-site Swelling	34.4			
Grade 3 injection-site Swelling	2.9			
Fever	35.9			
Grade 3 Fever	0.6			
Vomiting	37			
Grade 3 Vomiting	1.4			

Appetite Lost	43.5			
Grade 3 Appetite Lost	1.7			
Irritability	45.8			
Grade 3 Irritability	3			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Infant Subjects with Solicited Injection-site and Systemic Reactions After Each Injection with DTacP-IPV//PRP~T Combined Vaccine (Pentaxim®) Given as a Three-Dose Primary Vaccination.

End point title	Percentage of Infant Subjects with Solicited Injection-site and Systemic Reactions After Each Injection with DTacP-IPV//PRP~T Combined Vaccine (Pentaxim®) Given as a Three-Dose Primary Vaccination.[2]

End point description:

Solicited injection-site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever (temperature), Vomiting, Crying abnormal, Drowsiness, Appetite Lost, and Irritability.
Grade 3 injection-site: Tenderness, Cries when injected limb is moved, or the movement of the injected limb is reduced; Erythema and Swelling > 30 mm. Grade 3: Fever, > 39°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; and Irritability, Inconsolable.

End point type	Primary

End point timeframe:

Day 0 up Day 7 post-each vaccination

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 was performed based on the study vaccine administered for this outcome.

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	900			
Units: Percentage of Subjects				
number (not applicable)				
Injection-site Tenderness (Post-first injection)	27.7			
Grade 3 Inj-site Tenderness (Post-first injection)	0.4			
Injecting-site Tenderness (Post-second injection)	24.1			
Grade 3 Inj.-site Tenderness (Post-second inj.)	0.5			
Injecting-site Tenderness (Post-third injection)	23.6			
Grade 3 Inj.-site Tenderness (Post-third inj.)	0.5			
Injecting-site Swelling (Post-first injection)	10.6			
Grade 3 Injecting-site Swelling (Post-first inj.)	0.9			

Injecting-site Swelling (Post-second injection)	22.4			
Grade 3 Injecting-site Swelling (Post-second inj.)	1.7			
Injecting-site Swelling (Post-third injection)	24.2			
Grade 3 Injecting-site Swelling (Post-third inj.)	0.8			
Injecting-site Erythema (Post-first injection)	14.1			
Grade 3 Injecting-site Erythema (Post-first inj.)	0.3			
Injecting-site Erythema (Post-second injection)	29.9			
Grade 3 Injecting-site Erythema (Post-second inj.)	0.5			
Injecting-site Erythema (Post-third injection)	33			
Grade 3 Injecting-site Erythema (Post-third inj.)	0.7			
Fever (Post-first injection)	20.5			
Grade 3 Fever (Post-first injection)	0.1			
Fever (Post-second injection)	14.8			
Grade 3 Fever (Post-second injection)	0.2			
Fever (Post-third injection)	15			
Grade 3 Fever (Post-third injection)	0.2			
Vomiting (Post-first injection)	29.1			
Grade 3 Vomiting (Post-first injection)	1			
Vomiting (Post-second injection)	17.5			
Grade 3 Vomiting (Post-second injection)	0.2			
Vomiting (Post-third injection)	11.7			
Grade 3 Vomiting (Post-third injection)	0.5			
Crying Abnormal (Post-first injection)	40.6			
Grade 3 Crying Abnormal (Post-first injection)	2.3			
Crying Abnormal (Post-second injection)	37.1			
Grade 3 Crying Abnormal (Post-second injection)	1.7			
Crying Abnormal (Post-third injection)	26.6			
Grade 3 Crying Abnormal (Post-third injection)	1.4			
Drowsiness (Post-first injection)	35.2			
Grade 3 Drowsiness (Post-first injection)	1.1			
Drowsiness (Post-second injection)	24.1			
Grade 3 Drowsiness (Post-second injection)	0.5			
Drowsiness (Post-third injection)	19			
Grade 3 Drowsiness (Post-third injection)	0.3			
Appetite Lost (Post-first injection)	26.8			
Grade 3 Appetite Lost (Post-first injection)	0.7			
Appetite Lost (Post-second injection)	23.3			
Grade 3 Appetite Lost (Post-second injection)	0.8			
Appetite Lost (Post-third injection)	19			

Grade 3 Appetite Lost (Post-third injection)	0.5			
Irritability (Post-first injection)	30.6			
Grade 3 Irritability (Post-first injection)	1.4			
Irritability (Post-second injection)	26.8			
Grade 3 Irritability (Post-second injection)	1.4			
Irritability (Post-third injection)	20.9			
Grade 3 Irritability (Post-third injection)	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were reported from Day 0 (post-vaccination) up to Day 42 post-third vaccination.	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0
Reporting groups	
Reporting group title	Study Group
Reporting group description:	
Subjects received DTacP-IPV//PRP~T Combined Vaccine (Pentaxim®) as a three-dose primary vaccination at 2, 3, and 4 Months of Age.	

Serious adverse events	Study Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 900 (1.78%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Congenital, familial and genetic disorders			
Dermoid cyst			
subjects affected / exposed	1 / 900 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	1 / 900 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 900 (0.22%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			

subjects affected / exposed	6 / 900 (0.67%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Laryngitis			
subjects affected / exposed	1 / 900 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	3 / 900 (0.33%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 900 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pharyngitis			
subjects affected / exposed	1 / 900 (0.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Study Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	539 / 900 (59.89%)		
Nervous system disorders			
Drowsiness			
subjects affected / exposed	445 / 900 (49.44%)		
occurrences (all)	445		
Crying Abnormal			
subjects affected / exposed	539 / 900 (59.89%)		
occurrences (all)	539		
General disorders and administration site conditions			

Injection-site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	371 / 900 (41.22%)		
occurrences (all)	371		
Injection-site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	401 / 900 (44.56%)		
occurrences (all)	401		
Injection-site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	309 / 900 (34.33%)		
occurrences (all)	309		
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	322 / 900 (35.78%)		
occurrences (all)	322		
Irritability			
subjects affected / exposed	411 / 900 (45.67%)		
occurrences (all)	411		
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	332 / 900 (36.89%)		
occurrences (all)	332		
Metabolism and nutrition disorders			
Appetite Lost			
subjects affected / exposed	391 / 900 (43.44%)		
occurrences (all)	391		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None.

Notes: