Clinical trial results:
Immunogenicity and Safety of the sanofi pasteur's DTacP-IPV Combined Vaccine (TETRAXIM™) given as a booster dose at 4 to 6 years of life in children previously vaccinated with PENTAXIM™ in the study E2I34

Summary

EudraCT number	2015-005403-87
Trial protocol	Outside EU/EEA
Global end of trial date	31 May 2010

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	E2I57

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01031303
WHO universal trial number (UTN)	U1111-1112-2680

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur, SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon cedex 07, France, F-69367
Public contact	Medical Team Leader, Sanofi Pasteur, SA, 33 4 37 65 67 99, Emmanuel.vidor@sanofipasteur.com
Scientific contact	Medical Team 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	16 September 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 May 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess immunogenicity in terms of seroprotection rates (Diphtheria, Tetanus, Polio types 1, 2 and 3) and seroconversion/vaccine response rates to acellular Pertussis antigens (PT, FHA) of sanofi pasteur's DTacP-IPV (Tetraxim™) vaccine, one month after the booster dose given at 4 to 6 years of age.

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:

Subjects were vaccinated with PENTAXIM™ in a previous Study, 2015-005352-10 .

Evidence for comparator:

Not applicable.

Actual start date of recruitment	19 December 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Thailand: 123
Worldwide total number of subjects	123
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)	123
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 19 December 2009 to 31 March 2010 at 2 clinical centers in Thailand.

Pre-assignment

Screening details:

Subjects who received Sanofi Pasteur's DTacP-IPV//PRP~T vaccine (Pentaxim™) as a 3-dose primary vaccination (at 2, 4, and 6 months of age) in parallel with a recombinant hepatitis B vaccination received at birth, 2 and 6 months of age in the study E2I34 are eligible for the booster dose study.

Period 1

Period 1 title	Overall Study (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 a booster dose of study vaccine DTacP-IPV vaccine (TETRAXIM™) at 4 to 6 years of age (at visit 1).

Arm type	Experimental
Investigational medicinal product name	DTacP-IPV combined vaccine
Investigational medicinal product code	
Other name	TETRAXIM™
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, Intramuscular into the right deltoid region

Number of subjects in period 1	Study Group
Started	123
Completed	123

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	123	123	
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)	123	123	
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	4.2		
standard deviation	± 0.1	-	
Gender categorical Units: Subjects			
Female	50	50	
Male	73	73	

End points

End points reporting groups	
5HSRUWLQJ JURXS WLWOH	6WXG\ *URXS
5HSRUWLQJ JURXS GHVFULSWLRQ 6XEMHFWV UHFHLYHG D ERRVWHU GRVH RI VWXG\ YDFFLQH '7DF3 ,39 YDFFLQH DJH DW YLVLW	

Primary: Percentage of Subjects with Seroprotection, Seroconversion/Vaccine Response After Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in a Previous Study (2015-005352-10).

(QG SRLQW WLWOH	3HUFHQWDJH RI 6XEMHFWV ZLWK 6HURSURWHFWLRQ 6HURFRQYHUVLRQ 9DFFLQH 5HVSRQVH $IWHU %RRV ZLWK '7DF3 ,39 &RPELQHG 9DFFLQH 7(75$;,0Œ)RO 3ULPDU\ 3(17$;,0Œ 9DFFLQDWLRQ LQ D 3UHYLRXV 6 > @
(QG SRLQW GHVFULSWLRQ $QWL GLSKWKHULD ' DQG $QWL SROLRYLUXV ,39 W\SHV DQG DQWLERG QHXWUDOL]DWLRQ WHVW $QWL 7HWDQXV 7 DQWL 3HUWXVVLV WR[RLG 37 D)+$ DQWLERGLHV ZHUH PHDVXUHG E\ HQ]\PH OLQNHG LPPXQRVRUEHQW DVVD\	
(QG SRLQW W\SH	3ULPDU\
(QG SRLQW WLPHIUDPH 'D\ SRVW ERRVWHU YDFFLQDWLRQ	
1RWHV > @ 1R VWDWLVWLFDO DQDO\VHV KDYH EHHQ VSHFLILHG IRU WKLV SULPDU\ H OHDVW RQH VWDWLVWLFDO DQDO\VLV IRU HDFK SULPDU\ HQG SRLQW -XVWLILFDWLRQ 'HVFULSWLYH DQDO\VHV ZHUH SHUIRUPHG EDVHG RQ WKH ERR VWXG\	

End point values	6WXG\ *URXS		
6XEMHFW JURXS W\SH	5HSRUWLQJ JURXS		
1XPEHU RI VXEMHFWV DQDO\VHG			
8QLWV 3HUFHQWDJH RI 6XEMHFWV			
QXPEHU QRW DSSOLFDEOH			
$QWL 'LSKWHULD $QWL 7HWDQXV $QWL 3RLR $QWL 3RLR VXEMHFWV JRW 239 1 $QWL 3RLR VXEMHFWV GLG QRW JHW 239 1			
$QWL 3RLR $QWL 3RLR VXEMHFWV JRW 239 1 $QWL 3RLR VXEMHFWV GLG QRW JHW 239 1			
$QWL 3RLR $QWL 3RLR VXEMHFWV JRW 239 1 $QWL 3RLR VXEMHFWV GLG QRW JHW 239 1			
$QWL 3HUWXVVLV WR[RLG $QWL)LODPHQWRXV +DHPDJJOXWLQLQ			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers of Antibodies Against Vaccine Antigens Before and After Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in a Previous Study (2015-005352-10).

End point title	Geometric Mean Titers of Antibodies Against Vaccine Antigens Before and After Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in a Previous Study (2015-005352-10).

End point description:

Anti-diphtheria (D) and Anti-poliovirus (IPV) types 1, 2, and 3 antibodies were measured by a toxin neutralization test. Anti-Tetanus (T), anti-Pertussis toxoid (PT) and anti-Filamentous Haemagglutinin (FHA) antibodies were measured by enzyme-linked immunosorbent assay (ELISA)

End point type	Secondary

End point timeframe:

Day 0 Pre-vaccination and Day 30 Post-vaccination

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Diphtheria Antibody (Day 0 Pre-vaccination)	0.149 (0.109 to 0.204)			
Anti-Diphtheria Antibody (Day 30 Post-vaccination)	7.81 (6.47 to 9.43)			
Anti-Tetanus Antibody (Day 0 Pre-vaccination)	0.654 (0.556 to 0.769)			
Anti-Tetanus Antibody (Day 30 Post-vaccination)	7.72 (6.83 to 8.72)			
Anti-Polio 1 Antibody (Day 0 Pre-vaccination)	583 (467 to 729)			
Anti-Polio 1 Antibody (Day 30 Post-vaccination)	3013 (2631 to 3450)			
Anti-Polio 2 Antibody (Day 0 Pre-vaccination)	714 (566 to 900)			
Anti-Polio 2 Antibody (Day 30 Post-vaccination)	3430 (2969 to 3963)			
Anti-Polio 3 Antibody (Day 0 Pre-vaccination)	481 (374 to 619)			
Anti-Polio 3 Antibody (Day 30 Post-vaccination)	3837 (3261 to 4515)			

Anti-Pertussis Antibody (Day 0 Pre-vaccination)	10.9 (9.11 to 13.1)			
Anti-Pertussis Antibody (Day 30 Post-vaccination)	190 (168 to 216)			
Anti-FHA Antibody (Day 0 Pre-vaccination)	24.3 (19.7 to 29.9)			
Anti-FHA Antibody (Day 30 Post-vaccination)	356 (314 to 405)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Before and After Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in a Previous Study (2015-005352-10).

End point title	Geometric Mean Titer Ratios of Antibodies Against Vaccine Antigens Before and After Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in a Previous Study (2015-005352-10).

End point description:

Anti-diphtheria (D) and Anti-poliovirus (IPV) types 1, 2, and 3 antibodies were measured by a toxin neutralization test. Anti-Tetanus (T), anti-Pertussis toxoid (PT) and anti-Filamentous Haemagglutinin (FHA) antibodies were measured by enzyme-linked immunosorbent assay (ELISA)

End point type	Secondary

End point timeframe:

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

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: Titer Ratios				
geometric mean (confidence interval 95%)				
Anti-Diphtheria	52.5 (42.5 to 64.9)			
Anti-Tetanus	11.6 (10 to 13.5)			
Anti-Polio 1	5.14 (4.08 to 6.46)			
Anti-Polio 2	4.77 (3.82 to 5.96)			
Anti-Polio 3	8.26 (6.33 to 10.8)			
Anti-Pertussis toxoid	17.4 (15.1 to 20)			
Anti-Filamentous Haemagglutinin	14.6 (12.3 to 17.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Solicited Injection-site and Systemic Reactions After A Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in a Previous Study (2015-005352-10)

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions After A Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in a Previous Study (2015-005352-10)

End point description:

Solicited injection site reactions: Pain, Erythema, and Swelling. Solicited systemic reactions: Fever (temperature), Headache, Malaise, Myalgia, and Asthenia
Grade 3 injection-site Pain, Incapacitating, preventing the performance of usual activities; Erythema and Swelling, ≥5 cm; Fever, ≥39.0°C; Headache, Malaise, and Myalgia, Significant, prevents daily activity.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-vaccination

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: Percentage of Subjects				
number (not applicable)				
Injection-site Pain	75.6			
Grade 3 Injection-site Pain	0.8			
Injection-site Erythema	48.8			
Grade 3 Injection-site Erythema	4.1			
Injection-site Swelling	36.6			
Grade 3 Injection-site Swelling	2.4			
Fever	10.6			
Grade 3 Fever	0.8			
Headache	24.4			
Grade 3 Headache	0			
Malaise	32.5			
Grade 3 Malaise	0			
Myalgia	43.9			
Grade 3 Myalgia	0			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers of Antibodies Against Poliovirus Antigens Before and After Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in OPV and non-OPV Recipients in a Previous Study.

End point title	Geometric Mean Titers of Antibodies Against Poliovirus Antigens Before and After Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in OPV and non-OPV Recipients in a Previous Study.

End point description:

Geometric Mean Titers were determined in subjects who received Oral Polio Vaccine (OPV), and those who did not received Oral Polio Vaccine (N/A)
Anti-poliovirus (IPV) types 1, 2, and 3 antibodies was measured by a toxin neutralization test.

End point type	Other pre-specified

End point timeframe:

Day 0 (pre-vaccination) and Day 30 Post-vaccination.

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	123[2]			
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1 (Day 0, + OPV)	563 (296 to 1070)			
Anti-Polio 1 (Day 30, + OPV)	2719 (1752 to 4221)			
Anti-Polio 1 (Day 0, N/A)	586 (461 to 744)			
Anti-Polio 1 (Day 30, N/A)	3043 (2634 to 3516)			
Anti-Polio 2 (Day 0, + OPV)	875 (406 to 1885)			
Anti-Polio 2 (Day 30, + OPV)	3285 (1835 to 5881)			
Anti-Polio 2 (Day 0, N/A)	700 (547 to 895)			
Anti-Polio 2 (Day 30, N/A)	3444 (2961 to 4006)			
Anti-Polio 3 (Day 0, + OPV)	724 (315 to 1666)			
Anti-Polio 3 (Day 30, + OPV)	2896 (1758 to 4772)			
Anti-Polio 3 (Day 0, N/A)	462 (354 to 603)			
Anti-Polio 3 (Day 30, N/A)	3945 (3318 to 4692)			

Notes:

[2] - N = 11 for subject who received OPV (+ OPV)
N = 112 for subject who did not receive OPV (N/A)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titer Ratios of Antibodies Against Poliovirus Antigens Before and After Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in OPV and non-OPV Recipients in a Previous Study.

End point title	Geometric Mean Titer Ratios of Antibodies Against Poliovirus Antigens Before and After Booster Vaccination with DTacP-IPV Combined Vaccine (TETRAXIM™) Following Primary PENTAXIM™ Vaccination in OPV and non-OPV Recipients in a Previous Study.

End point description:

Geometric Mean Titers were determined in subjects who received Oral Polio Vaccine (OPV), and those who did not received Oral Polio Vaccine (N/A)
Anti-poliovirus (IPV) types 1, 2, and 3 antibodies were measured by a toxin neutralization test.

End point type	Other pre-specified

End point timeframe:

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

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	123[3]			
Units: Titer Ratios				
geometric mean (confidence interval 95%)				
Anti-polio 1 (Day 30 + OPV)	4.83 (1.91 to 12.2)			
Anti-polio 1 (Day 30, N/A)	5.17 (4.07 to 6.57)			
Anti-polio 2 (Day 30 + OPV)	3.76 (1.79 to 7.89)			
Anti-polio 2 (Day 30 , N/A)	4.88 (3.85 to 6.19)			
Anti-polio 3 (Day 30 + OPV)	4 (1.55 to 10.3)			
Anti-polio 2 (Day 30, N/A)	8.88 (6.72 to 11.7)			

Notes:

[3] - N = 11 for subject who received OPV (+ OPV)
N = 112 for subject who did not receive OPV (N/A)

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 up to Day 30 post-vaccination	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1
Reporting groups	
Reporting group title	Study Group
Reporting group description:	
Subjects received a booster dose of study vaccine DTacP-IPV vaccine (TETRAXIM™) at 4 to 6 years of age (at visit 1).	

Serious adverse events	Study Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 123 (0.81%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 123 (0.81%)		
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	93 / 123 (75.61%)		
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 123 (24.39%)		
occurrences (all)	30		
General disorders and administration site conditions			

Injection site Pain alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 93 / 123 (75.61%) 93		
Injection-site Erythema alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 60 / 123 (48.78%) 60		
Injection-site Swelling alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 45 / 123 (36.59%) 45		
Fever alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 13 / 123 (10.57%) 13		
Malaise alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 40 / 123 (32.52%) 40		
Musculoskeletal and connective tissue disorders			
Myalgia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 54 / 123 (43.90%) 54		
Infections and infestations			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	 28 / 123 (22.76%) 30		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 October 2009	This amendment was issued before the commencement of the trial to change the site of the intramuscular injection of the vaccine from anterolateral aspect of the right thigh to the right deltoid region.
13 January 2010	Protocol updated to allow inclusion of subjects that received or were to receive Oral Polio Vaccine (OPV) as part of the National Immunization Days (that occurred at the same time as study period in Thailand) In the section on "Population used in the Analyses" the following text was added "In addition, anti polio 1, 2, and 3 antibody titers will be analyzed on the subset of subjects who did not receive OPV as part of the National Immunization Days campaign, as well as on the subset of subjects who received OPV as part of the National Immunization Days campaign."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported