Clinical trial results:
Immunogenicity and Safety of ADACEL Polio (TdcP-IPV Vaccine) Administered at 6 to 8 Years of Age as a Fifth Dose (Pre-School Booster) in Healthy Children in Taiwan

Summary

EudraCT number	2015-005190-21
Trial protocol	Outside EU/EEA
Global end of trial date	09 April 2009

Results information

Result version number	v1 (current)
This version publication date	18 February 2016
First version publication date	18 February 2016

Trial information

Trial identification

Sponsor protocol code	TD525

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00797511
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	Medical Director Franchise, Sanofi Pasteur SA, 33 4 37 37 70 82, RegistryContactUS@sanofipasteur.com
Scientific contact	Medical Director Franchise, Sanofi Pasteur SA, 33 4 37 37 70 82, 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	03 August 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 April 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To describe the immunogenicity profile of ADACEL Polio (TdcP-IPV vaccine) one month after administration.

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:

ADACEL Polio was administered as a fifth dose following complete primary series and fourth dose of diphtheria, tetanus, pertussis vaccine and polio vaccines.

Evidence for comparator:

Not applicable

Actual start date of recruitment	24 November 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	Taiwan: 132
Worldwide total number of subjects	132
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)	132
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 24 November 2008 to 11 March 2009 at 1 medical center in Taiwan.

Pre-assignment

Screening details:

A total of 132 subjects who met the inclusion and none of the exclusion criteria were enrolled, vaccinated, and evaluated.

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	Adacel Polio Vaccine Study Group

Arm description:

Subjects received one dose of TdcP-IPV vaccine (ADACEL Polio).

Arm type	Experimental
Investigational medicinal product name	Tetanus, diphtheria (reduced antigen content), pertussis (acellular components) vaccine
Investigational medicinal product code	TdcP-IPV
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular in the left deltoid, 1 injection on Day 0.

Number of subjects in period 1	Adacel Polio Vaccine Study Group
Started	132
Completed	131
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	Adacel Polio Vaccine Study Group
Reporting group description:	
Subjects received one dose of TdcP-IPV vaccine (ADACEL Polio).	

Reporting group values	Adacel Polio Vaccine Study Group	Total	
Number of subjects	132	132	
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)	132	132	
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	6.89		
standard deviation	± 0.3	-	
Gender categorical			
Units: Subjects			
Female	64	64	
Male	68	68	

End points

End points reporting groups

Reporting group title	Adacel Polio Vaccine Study Group
Reporting group description:	
Subjects received one dose of TdcP-IPV vaccine (ADACEL Polio).	

Primary: Number of Subjects With Seroprotection to Vaccine Antigens Following Vaccination With ADACEL Polio (TdcP-IPV) Vaccine

End point title	Number of Subjects With Seroprotection to Vaccine Antigens Following Vaccination With ADACEL Polio (TdcP-IPV) Vaccine[1]
End point description:	
Diphtheria concentrations determined by diphtheria toxin neutralization assay (Dip SN); Tetanus concentrations determined by enzyme-linked immunosorbent assay (ELISA). Seroprotection titer levels were defined as anti-diphtheria antibody titers ≥0.1 international unit (IU) per milliliter (mL), anti-tetanus antibody titers ≥0.01 IU/mL and ≥0.1 IU/mL, and anti-polio (≥8 1/dilution).	
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 groups and the study vaccine administered for this outcome.

End point values	Adacel Polio Vaccine Study Group			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: Number of subjects				
number (not applicable)				
Anti-Diphtheria (post-vaccination)	131			
Anti-Tetanus (post-vaccination)	131			
Anti-Polio 1 (post-vaccination)	131			
Anti-Polio 2 (post-vaccination)	131			
Anti-Polio 3 (post-vaccination)	131			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Booster Response to Vaccine Pertussis Antigens Following Vaccination With ADACEL Polio (TdcP-IPV) Vaccine

End point title	Number of Subjects With Booster Response to Vaccine Pertussis Antigens Following Vaccination With ADACEL Polio (TdcP-IPV) Vaccine[2]
End point description:	
The anti-Pertussis concentration was determined by ELISA. The criteria for demonstrating booster response were: (i) Pre-vaccination antibody concentrations less than the lower limit of quantitation	

(LLOQ) for each anti-pertussis antibody (pertussis toxoid [PT], filamentous hemagglutinin [FHA], fimbriae [FIM] types 2 and 3, and pertactin [PRN]) but post-vaccination levels ≥4X LLOQ, or (ii) Pre-vaccination antibody concentrations ≥LLOQ but <4X LLOQ with a 4-fold rise rate, or (iii) Pre-vaccination antibody concentrations ≥4X LLOQ but with a 2-fold rise rate.

End point type	Primary

End point timeframe:

Day 28 post-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 were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Adacel Polio Vaccine Study Group			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: Number of subjects				
number (not applicable)				
Anti-PT	88			
Anti-FHA	126			
Anti-FIM types 2 and 3	116			
Anti-PRN	130			

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Antibodies to ADACEL Polio Vaccine Antigens Following Vaccination

End point title	Geometric Mean Titers (GMTs) of Antibodies to ADACEL Polio Vaccine Antigens Following Vaccination[3]

End point description:

Diphtheria antibody concentrations determined by diphtheria toxin neutralization assay; Tetanus antibody concentrations determined by enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

Day 28 post-vaccination

Notes:

[3] - 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 groups and the study vaccine administered for this outcome.

End point values	Adacel Polio Vaccine Study Group			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				

Anti-Diphtheria (post-vaccination)	3.81 (3.25 to 4.46)			
Anti-Tetanus (post-vaccination)	17.2 (14.8 to 20)			
Anti-Polio 1 (post-vaccination)	9627 (7960 to 11642)			
Anti-Polio 2 (post-vaccination)	7083 (6057 to 8282)			
Anti-Polio 3 (post-vaccination)	9860 (8244 to 11793)			

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers of Antibodies to Pertussis Antigens Following Vaccination With ADACEL Polio Vaccine

End point title	Geometric Mean Titers of Antibodies to Pertussis Antigens Following Vaccination With ADACEL Polio Vaccine[4]

End point description:

Pre- and post-vaccination GMTs for the pertussis toxoid (PT), pertussis filamentous hemagglutinin (FHA), pertussis pertactin (PRN), and pertussis fimbriae types 2 and 3 (FIM) were all determined by enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

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

Notes:

[4] - 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 groups and the study vaccine administered for this outcome.

End point values	Adacel Polio Vaccine Study Group			
Subject group type	Reporting group			
Number of subjects analysed	131			
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Anti-PT (pre-vaccination)	4.53 (3.81 to 5.39)			
Anti-PT (post-vaccination)	42.7 (36.1 to 50.3)			
Anti-FHA (pre-vaccination)	19.7 (16.4 to 23.7)			
Anti-FHA (post-vaccination)	164 (145 to 185)			
Anti-FIM types 2 and 3 (pre-vaccination)	17.5 (12.8 to 24)			
Anti-FIM types 2 and 3 (post-vaccination)	423 (291 to 614)			
Anti-PRN (pre-vaccination)	11.9 (9.92 to 14.3)			
Anti-PRN (post-vaccination)	314 (263 to 376)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting at Least 1 Solicited Injection Site or Systemic Reaction Post-Vaccination With ADACEL Polio Vaccine

End point title	Number of Subjects Reporting at Least 1 Solicited Injection Site or Systemic Reaction Post-Vaccination With ADACEL Polio Vaccine

End point description:

Solicited Injection site reactions: Pain, Erythema, Swelling, and Extensive swelling of vaccinated limb. Solicited systemic reactions: Fever (Temperature), Headache, Malaise, and Myalgia. Grade 3 Injection site reactions: Pain, Incapacitating, unable to perform usual activities; Erythema and Swelling, ≥5 cm. By convention, extensive swelling of vaccinated limb is considered severe. Grade 3 Systemic reactions: Fever, >39.0°C; Headache, Malaise, and Myalgia, Prevents daily activities.

End point type	Secondary

End point timeframe:

Day 0 up to Day 7 post-vaccination

End point values	Adacel Polio Vaccine Study Group			
Subject group type	Reporting group			
Number of subjects analysed	132			
Units: Number of subjects				
number (not applicable)				
Any Solicited Injection Site Reaction	112			
Any Injection site Erythema	61			
Grade 3 Injection site Erythema	4			
Any Injection site Swelling	40			
Grade 3 Injection site Swelling	2			
Any Injection site Pain	102			
Grade 3 Injection site Pain	1			
Any extensive swelling of vaccinated limb	0			
Grade 3 Any extensive swelling of vaccinated limb	0			
Any Solicited Systemic Reaction	63			
Any Fever	14			
Grade 3 Fever	2			
Any Headache	28			
Grade 3 Headache	1			
Any Myalgia	46			
Grade 3 Myalgia	0			
Any Malaise	27			

Grade 3 Malaise	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-vaccination) up to 1 month post-vaccination.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups	
Reporting group title	Adacel Polio Vaccine Study Group
Reporting group description:	
Subjects received one dose of TdcP-IPV vaccine (ADACEL Polio).	

Serious adverse events	Adacel Polio Vaccine Study Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 132 (1.52%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	1 / 132 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 132 (0.76%)		
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	Adacel Polio Vaccine Study Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 132 (77.27%)		
Nervous system disorders			

Headache			
alternative assessment type: Systematic			
subjects affected / exposed	28 / 132 (21.21%)		
occurrences (all)	28		
General disorders and administration site conditions			
Injection site Pain			
alternative assessment type: Systematic			
subjects affected / exposed	102 / 132 (77.27%)		
occurrences (all)	102		
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	61 / 132 (46.21%)		
occurrences (all)	61		
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 132 (10.61%)		
occurrences (all)	14		
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 132 (20.45%)		
occurrences (all)	27		
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	40 / 132 (30.30%)		
occurrences (all)	40		
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	46 / 132 (34.85%)		
occurrences (all)	46		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	19 / 132 (14.39%)		
occurrences (all)	19		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 December 2008	Allowed Investigator the possibility to include potential subjects directly at the Hospital and not only through the schools in order to increase recruitment rate.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported