Clinical trial results:
Immunogenicity and Safety of the Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (SP306) as a Booster in Japanese Adolescents

Summary

EudraCT number	2015-005628-25
Trial protocol	Outside EU/EEA
Global end of trial date	11 November 2012

Results information

Result version number	v1 (current)
This version publication date	19 February 2016
First version publication date	19 February 2016

Trial information

Trial identification

Sponsor protocol code	Td540

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01689324
WHO universal trial number (UTN)	U1111-1124-7671

Notes:

Sponsors

Sponsor organisation name	Sanofi K.K.
Sponsor organisation address	3-20-2, Nishi Shinjuku, Shinjuku-ku, Tokyo, Japan, 163-1488
Public contact	Medical Director, Sanofi K.K, +81 3 6301 3603, Toshihiro.emori@sanofi.com
Scientific contact	Medical Director, Sanofi K.K, +81 3 6301 3603, Toshihiro.emori@sanofi.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 February 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunogenicity of Adacel (SP306) when administered as a single dose in Japanese adolescents.

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:

Subjects who were enrolled in the study were previously vaccinated with 4 doses of pediatric diphtheria, pertussis and tetanus (DTaP) vaccine.

Evidence for comparator:

Not applicable

Actual start date of recruitment	12 September 2012
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: 43
Worldwide total number of subjects	43
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)	25
Adolescents (12-17 years)	18
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 12 September 2012 through 14 October 2012 in 3 clinic centers in Japan.

Pre-assignment

Screening details:

A total of 43 subjects that met all the inclusion criteria but none of the exclusion criteria were enrolled and vaccinated in the study.

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	Study Group

Arm description:

Subjects received a single booster dose of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed (TDaP; Adacel®) intramuscularly.

Arm type	Experimental
Investigational medicinal product name	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Adacel®)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

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

Number of subjects in period 1	Study Group
Started	43
Completed	43

Baseline characteristics

Reporting groups	
Reporting group title	Study Group
Reporting group description:	
Subjects received a single booster dose of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed (TDaP; Adacel®) intramuscularly.	

Reporting group values	Study Group	Total	
Number of subjects	43	43	
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)	0	0	
Adolescents (12-17 years)	43	43	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	11.4		
standard deviation	± 0.5	-	
Gender categorical Units: Subjects			
Female	23	23	
Male	20	20	

End points

End points reporting groups

Reporting group title	Study Group

Reporting group description:

Subjects received a single booster dose of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed (TDaP; Adacel®) intramuscularly.

Primary: Percentage of Subjects With Seroprotection Against Diphtheria and Tetanus Antigens Following Vaccination With ADACEL®

End point title	Percentage of Subjects With Seroprotection Against Diphtheria and Tetanus Antigens Following Vaccination With ADACEL®[1]

End point description:

Seroprotection was defined as the percentage of subjects with antibody concentration levels ≥0.1 IU/mL post-vaccination.

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	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Percentage of subjects				
number (not applicable)				
Diphtheria	100			
Tetanus	100			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Booster Response to Diphtheria and Tetanus Antigens Following Vaccination With ADACEL®

End point title	Percentage of Subjects With Booster Response to Diphtheria and Tetanus Antigens Following Vaccination With ADACEL®[2]

End point description:

Diphtheria booster response was defined as a ≥ 4-fold rise in pre- to post-vaccination antitoxin concentration in a subject with a pre-vaccination antitoxin concentration ≤ 2.56 IU/mL; or a ≥ 2-fold rise in a subject with a pre-vaccination antitoxin concentration > 2.56 IU/mL.

Tetanus booster response was defined as a ≥ 4-fold rise in pre- to post-vaccination antitoxin concentration in a subject with a pre-vaccination antitoxin concentration ≤ 2.7 IU/mL; or a ≥ 2-fold rise in a subject with a pre-vaccination antitoxin concentration >2.7 IU/mL.

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	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Percentage of subjects				
number (not applicable)				
Diphtheria	98			
Tetanus	100			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Booster Response to Pertussis Antigens Following Vaccination with ADACEL®

End point title	Percentage of Subjects With Booster Response to Pertussis Antigens Following Vaccination with ADACEL®[3]

End point description:

Booster responses were defined as: Pre-vaccination antibody concentrations less than the lower limit of quantitation (LLOQ) and post-vaccination levels ≥ 4X LLOQ; or Pre-vaccination antibody concentrations ≥ LLOQ but < 4X LLOQ, and a 4-fold rise (i.e., post-/pre-vaccination ≥ 4), or Pre-vaccination antibody concentrations ≥ 4X LLOQ and a 2-fold rise (i.e., post-/pre-vaccination ≥ 2).

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	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Percentage of subjects				
number (not applicable)				
Pertussis toxoid	63			
Filamentous hemagglutinin	88			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Seroprotection Against Diphtheria and Tetanus Antigens Pre-Vaccination With ADACEL®

End point title	Percentage of Subjects With Seroprotection Against Diphtheria and Tetanus Antigens Pre-Vaccination With ADACEL®

End point description:

Seroprotection was defined as the percentage of subjects with antibody concentration of ≥ 0.1 IU/mL.

End point type	Other pre-specified

End point timeframe:

Day 0 pre-vaccination

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Percentage of subjects				
number (not applicable)				
Diphtheria	63			
Tetanus	91			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Seroprotection Against Diphtheria and Tetanus Antigens Pre-Vaccination and Post-Vaccination With ADACEL®

End point title	Percentage of Subjects With Seroprotection Against Diphtheria and Tetanus Antigens Pre-Vaccination and Post-Vaccination With ADACEL®

End point description:

Seroprotection was defined as the percentage of subjects with antibody concentration of ≥ 0.01 IU/mL.

End point type	Other pre-specified

End point timeframe:

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

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Percentage of subjects				
number (not applicable)				
Diphtheria (pre-vaccination)	100			
Diphtheria (post-vaccination)	100			
Tetanus (pre-vaccination)	100			
Tetanus (post-vaccination)	100			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Seroprotection Against Diphtheria and Tetanus Antigens Pre-Vaccination and Post-Vaccination With ADACEL®

End point title	Percentage of Subjects With Seroprotection Against Diphtheria and Tetanus Antigens Pre-Vaccination and Post-Vaccination With ADACEL®

End point description:

Seroprotection was defined as the percentage of subjects with antibody concentrations ≥ 1.0 IU/mL.

End point type	Other pre-specified

End point timeframe:

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

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Percentage of subjects				
number (not applicable)				
Diphtheria (pre-vaccination)	12			
Diphtheria (post-vaccination)	100			
Tetanus (pre-vaccination)	30			
Tetanus (post-vaccination)	100			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Concentrations With Respect to Diphtheria and Tetanus Antibodies Pre- and Post-Vaccination with ADACEL®

End point title	Geometric Mean Concentrations With Respect to Diphtheria and Tetanus Antibodies Pre- and Post-Vaccination with ADACEL®

End point description:

End point type	Other pre-specified

End point timeframe:

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

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Diphtheria (pre-vaccination)	0.22 (0.14 to 0.35)			
Diphtheria (post-vaccination)	8.58 (6.76 to 10.88)			
Tetanus (pre-vaccination)	0.46 (0.33 to 0.64)			
Tetanus (post-vaccination)	37.8 (30.16 to 47.38)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Concentrations With Respect to Pertussis Antibodies Pre- and Post-Vaccination with ADACEL®

End point title	Geometric Mean Concentrations With Respect to Pertussis Antibodies Pre- and Post-Vaccination with ADACEL®

End point description:

Pertussis immune response was measured using Japanese standard enzyme-linked immunosorbent assay.

End point type	Other pre-specified

End point timeframe:

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

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Pertussis toxoid (pre-vaccination)	12.21 (7.82 to 19.05)			
Pertussis toxoid (post-vaccination)	46.92 (33.65 to 65.42)			
Filamentous hemagglutinin (pre-vaccination)	34.79 (23.47 to 51.57)			
Filamentous hemagglutinin (post-vaccination)	204 (164.26 to 253.36)			
Pertactin (pre-vaccination)	10.64 (6.28 to 18.03)			

Pertactin (post-vaccination)	272.82 (197.63 to 376.62)			
Fimbriae types 2 and 3 (pre-vaccination)	7.78 (5.42 to 11.17)			
Fimbriae types 2 and 3 (post-vaccination)	748.28 (443.23 to 1263.27)			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects With Booster Response to Pertussis Antigens Following Vaccination with ADACEL®

End point title	Percentage of Subjects With Booster Response to Pertussis Antigens Following Vaccination with ADACEL®

End point description:

Booster responses were defined as: Pre-vaccination antibody concentrations less than the lower limit of quantitation (LLOQ) and a post-vaccination level ≥ 4X LLOQ; or Pre-vaccination antibody concentrations ≥ LLOQ but < 4X LLOQ, and a 4-fold rise (i.e., post-/pre-vaccination ≥ 4), or Pre-vaccination antibody concentrations ≥ 4X LLOQ and a 2-fold rise (i.e., post-/pre-vaccination) ≥ 2).

End point type	Other pre-specified

End point timeframe:

Day 28 post-vaccination

End point values	Study Group			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Percentage of subjects				
number (not applicable)				
Pertactin	93			
Fimbriae Types 2 and 3	98			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects Reporting Solicited Injection Site and Systemic Reactions Following Vaccination With ADACEL®

End point title	Number of Subjects Reporting Solicited Injection Site and Systemic Reactions Following Vaccination With ADACEL®

End point description:

Solicited injection site reactions: Pain, Erythema, and Swelling. Grade 3: Pain, Significant, prevents daily activity; Erythema and Swelling, > 100 mm.

Solicited systemic reactions: Fever (Temperature), Headache, Malaise, and Myalgia. Grade 3: Fever, ≥ 39°C; Headache, Malaise, and Myalgia, Significant, prevents daily activity.

End point type	Other pre-specified

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	43			
Units: Number of subjects				
number (not applicable)				
Solicited Injection site Pain	37			
Grade 3 Solicited Injection site Pain	0			
Solicited Injection site Erythema	9			
Grade 3 Solicited Injection site Erythema	0			
Solicited Injection site Swelling	12			
Grade 3 Solicited Injection site Swelling	1			
Fever	9			
Grade 3 Fever	1			
Headache	8			
Grade 3 Headache	0			
Malaise	11			
Grade 3 Malaise	0			
Myalgia	17			
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-vaccination) up to 1 month post-vaccination.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	Study Group
Reporting group description:	
Subjects received a single booster dose of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed (TDaP; Adacel®) intramuscularly.	

Serious adverse events	Study Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 43 (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	Study Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 43 (90.70%)		
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 43 (18.60%)		
occurrences (all)	8		
General disorders and administration site conditions			
Injection site Pain			
alternative assessment type: Systematic			
subjects affected / exposed	37 / 43 (86.05%)		
occurrences (all)	37		
Injection site Erythema			

alternative assessment type: Systematic subjects affected / exposed occurrences (all) Injection site Swelling alternative assessment type: Systematic subjects affected / exposed occurrences (all) Fever alternative assessment type: Systematic subjects affected / exposed occurrences (all) Malaise alternative assessment type: Systematic subjects affected / exposed occurrences (all)	9 / 43 (20.93%) 9 12 / 43 (27.91%) 12 9 / 43 (20.93%) 9 11 / 43 (25.58%) 11		
Musculoskeletal and connective tissue disorders Myalgia alternative assessment type: Systematic subjects affected / exposed occurrences (all)	17 / 43 (39.53%) 17		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 43 (16.28%) 9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 November 2012	Revised observational endpoints and immunogenicity assessment methods to note that the pertussis immune response would be characterized by a Japanese laboratory using a enzyme-linked immunosorbent assay kit, and updated the storage and shipment procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported