Clinical trial results:
Immunogenicity and Safety of Sanofi Pasteur's Tdap Combined Vaccine (ADACEL) as a Booster Dose, versus Local DT Vaccine in Healthy Children or versus Local Td Vaccine in Healthy Adolescents and Adults in China

Summary

EudraCT number	2015-003941-24
Trial protocol	Outside EU/EEA
Global end of trial date	07 January 2014

Results information

Result version number	v1 (current)
This version publication date	24 April 2016
First version publication date	24 April 2016

Trial information

Trial identification

Sponsor protocol code	Td528

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01993173
WHO universal trial number (UTN)	U1111-1127-7835

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Limited, China
Sponsor organisation address	6th Floor, No. 112 Jian Guo Lu, Chaoyang District, Beijing, China, 100022
Public contact	Director, Clinical Development, Sanofi Pasteur Limited, China, 86 10 6563 8188, Jean-denis.shu@sanofipasteur.com
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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	24 April 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe diphtheria and tetanus seroprotection rates and pertussis booster response rates induced by each of the study vaccines: ADACEL vaccine (in all study age groups), local DT vaccine (in children), and local Td vaccine (in adolescents and adults)

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:

All subjects enrolled in the Td528 study had previously completed primary series and fourth dose of diphtheria, tetanus, and pertussis (DTP) vaccine.

Evidence for comparator:

Not applicable

Actual start date of recruitment	18 November 2013
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: 1439
Worldwide total number of subjects	1439
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)	719
Adolescents (12-17 years)	141

Adults (18-64 years)	579
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study subjects were enrolled from 18 November 2013 to 07 December 2013 at 1 clinic center in China.

Pre-assignment

Screening details:

A total of 1440 subjects who met all inclusion and none of the exclusion criteria were randomized, 1439 subjects were vaccinated in this study.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

This study was conducted in an observer-blind manner. The Investigator, and blinded staff in charge of safety assessment, did not know which vaccine was administered. Subjects/parents also remained blinded and were unaware of the vaccine assignment. To maintain the blind, the vaccine was prepared in a separate room as well as the safety assessment. In the event of an emergency, i.e., serious adverse event, the code could be broken by the Investigator as described in the code-breaking procedures.

Arms

Are arms mutually exclusive?	Yes
Arm title	ADACEL 4-11 Years

Arm description:

Subjects 4 to 11 years of age received a single booster dose of ADACEL (Tdap vaccine).

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, 1 single booster dose on Day 0.

Arm title	ADACEL 12-64 Years

Arm description:

Subjects 12 to 64 years of age received a single booster dose of ADACEL (Tdap vaccine).

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, 1 single booster dose on Day 0.

Arm title	Local DT 4-11 Years

Arm description:	
Subjects 4-11 years of age received a single booster dose of local DT vaccine.	
Arm type	Active comparator
Investigational medicinal product name	DT vaccine (Diphtheria and Tetanus Combined Vaccine, Adsorbed)
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 deltoid, 1 single booster dose on Day 0.	
Arm title	Local Td 12-64 Years
Arm description:	
Subjects 12-64 years of age received a single booster dose of local Td vaccine.	
Arm type	Active comparator
Investigational medicinal product name	Td vaccine (Diphtheria and Tetanus Combined Vaccine for Adults and Adolescents, Adsorbed)
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 deltoid, 1 single booster dose on Day 0.	

Number of subjects in period 1	ADACEL 4-11 Years	ADACEL 12-64 Years	Local DT 4-11 Years
Started	359	362	360
Completed	359	362	360

Number of subjects in period 1	Local Td 12-64 Years
Started	358
Completed	358

Baseline characteristics

Reporting groups	
Reporting group title	ADACEL 4-11 Years
Reporting group description:	
Subjects 4 to 11 years of age received a single booster dose of ADACEL (Tdap vaccine).	
Reporting group title	ADACEL 12-64 Years
Reporting group description:	
Subjects 12 to 64 years of age received a single booster dose of ADACEL (Tdap vaccine).	
Reporting group title	Local DT 4-11 Years
Reporting group description:	
Subjects 4-11 years of age received a single booster dose of local DT vaccine.	
Reporting group title	Local Td 12-64 Years
Reporting group description:	
Subjects 12-64 years of age received a single booster dose of local Td vaccine.	

Reporting group values	ADACEL 4-11 Years	ADACEL 12-64 Years	Local DT 4-11 Years
Number of subjects	359	362	360
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)	0	0	0
Children (2-11 years)	359	0	360
Adolescents (12-17 years)	0	71	0
Adults (18-64 years)	0	291	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	8.45	39.3	8.52
standard deviation	± 1.78	± 16.2	± 1.78
Gender categorical Units: Subjects			
Female	152	216	152
Male	207	146	208

Reporting group values	Local Td 12-64 Years	Total	
Number of subjects	358	1439	
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	719	
Adolescents (12-17 years)	70	141	
Adults (18-64 years)	288	579	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	38.9		
standard deviation	± 16.2	-	
Gender categorical			
Units: Subjects			
Female	217	737	
Male	141	702	

End points

End points reporting groups

Reporting group title	ADACEL 4-11 Years
Reporting group description:	
Subjects 4 to 11 years of age received a single booster dose of ADACEL (Tdap vaccine).	
Reporting group title	ADACEL 12-64 Years
Reporting group description:	
Subjects 12 to 64 years of age received a single booster dose of ADACEL (Tdap vaccine).	
Reporting group title	Local DT 4-11 Years
Reporting group description:	
Subjects 4-11 years of age received a single booster dose of local DT vaccine.	
Reporting group title	Local Td 12-64 Years
Reporting group description:	
Subjects 12-64 years of age received a single booster dose of local Td vaccine.	

Primary: Percentage of Subjects with Diphtheria and Tetanus Seroprotection and Pertussis Booster Response One Month After Booster Vaccination with ADACEL or Local DT or Local Td Vaccine

End point title	Percentage of Subjects with Diphtheria and Tetanus Seroprotection and Pertussis Booster Response One Month After Booster Vaccination with ADACEL or Local DT or Local Td Vaccine[1]

End point description:

Diphtheria and Tetanus antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA). Seroprotection was defined as Anti-Diphtheria or Anti-Tetanus antibody concentrations ≥ 0.1 IU/mL. Pertussis (Pertussis Toxoid, Filamentous hemagglutinin, Pertactin, and Fimbriae Types 2 and 3) booster response was defined as subjects with pre-vaccination antibody concentrations < lower limit of quantitation (LLOQ) if post-vaccination levels ≥ 4 x LLOQ, for subjects with pre-vaccination antibody concentrations ≥ LLOQ but < 4 x LLOQ if post-/pre-vaccination antibody concentrations ratio ≥ 4, for subjects with pre-vaccination antibody concentrations ≥ 4 x LLOQ if post-/pre-vaccination antibody concentrations ratio ≥ 2.

End point type	Primary

End point timeframe:

1 month post-booster 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 4-11 Years	ADACEL 12-64 Years	Local DT 4-11 Years	Local Td 12-64 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	354	362	354	357
Units: Percentage of subjects				
number (not applicable)				
Diphtheria seroprotection	99.7	99.2	100	100
Tetanus seroprotection	100	100	100	100
Pertussis Toxoid booster response	89.5	93.4	28.8	43.7
Filamentous hemagglutinin booster response	99.2	94.2	59.6	67.2
Pertactin booster response	80.2	89	44.4	9

Fimbriae Types 2 and 3 booster response	98.6	95.6	29.7	9.5

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions After Booster Vaccination with ADACEL or Local DT or Local Td Vaccine

End point title	Percentage of Subjects Reporting a Solicited Injection-site or Systemic Reactions After Booster Vaccination with ADACEL or Local DT or Local Td Vaccine

End point description:

Solicited Injection site reactions: Pain, Erythema, and Swelling. Solicited Systemic reactions: Fever (Temperature), Headache, Malaise, Myalgia.

Grade 3 Solicited Injection site reactions: Pain, Incapacitating, unable to perform usual activities; Erythema and Swelling, > 30 mm. Grade 3 Solicited Systemic reactions: 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-booster vaccination

End point values	ADACEL 4-11 Years	ADACEL 12-64 Years	Local DT 4-11 Years	Local Td 12-64 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	359	362	360	358
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Pain	42.6	44.5	35.6	39.4
Grade 3 Injection site Pain	0.3	0	0.6	0
Any Injection site Erythema	12.5	10.2	9.4	7
Grade 3 Injection site Erythema	1.1	0.6	0	0.3
Any Injection site Swelling	11.7	9.9	8.9	7.3
Grade 3 Injection site Swelling	3.1	1.1	0.3	0.8
Any Fever	9.7	6.6	11.9	6.4
Grade 3 Fever	0	0	0	0
Any Headache	6.7	8.6	6.7	6.4
Grade 3 Headache	0	0.3	0	0.3
Any Malaise	15	16.3	16.1	14
Grade 3 Malaise	0	0.3	0	0
Any Myalgia	18.7	19.1	15.6	14.5
Grade 3 Myalgia	0.6	0.3	0	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 up to 1 month post-booster vaccination.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16

Reporting groups	
Reporting group title	ADACEL 4-11 Years
Reporting group description:	
Subjects 4 to 11 years of age received a single booster dose of ADACEL (Tdap vaccine).	
Reporting group title	ADACEL 12-64 Years
Reporting group description:	
Subjects 12 to 64 years of age received a single booster dose of ADACEL (Tdap vaccine).	
Reporting group title	Local DT 4-11 Years
Reporting group description:	
Subjects 4-11 years of age received a single booster dose of local DT vaccine.	
Reporting group title	Local Td 12-64 Years
Reporting group description:	
Subjects 12-64 years of age received a single booster dose of local Td vaccine.	

Serious adverse events	ADACEL 4-11 Years	ADACEL 12-64 Years	Local DT 4-11 Years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 359 (0.00%)	0 / 362 (0.00%)	0 / 360 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Local Td 12-64 Years		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 358 (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	ADACEL 4-11 Years	ADACEL 12-64 Years	Local DT 4-11 Years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	153 / 359 (42.62%)	161 / 362 (44.48%)	128 / 360 (35.56%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 359 (6.69%)	31 / 362 (8.56%)	24 / 360 (6.67%)
occurrences (all)	24	31	24
General disorders and administration site conditions			
Injection site Pain			
alternative assessment type: Systematic			
subjects affected / exposed	153 / 359 (42.62%)	161 / 362 (44.48%)	128 / 360 (35.56%)
occurrences (all)	153	161	128
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	45 / 359 (12.53%)	37 / 362 (10.22%)	34 / 360 (9.44%)
occurrences (all)	45	37	34
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	42 / 359 (11.70%)	36 / 362 (9.94%)	32 / 360 (8.89%)
occurrences (all)	42	36	32
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 359 (9.75%)	24 / 362 (6.63%)	43 / 360 (11.94%)
occurrences (all)	35	24	43
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	54 / 359 (15.04%)	59 / 362 (16.30%)	58 / 360 (16.11%)
occurrences (all)	54	59	58
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	67 / 359 (18.66%)	69 / 362 (19.06%)	56 / 360 (15.56%)
occurrences (all)	67	69	56

Non-serious adverse events	Local Td 12-64 Years		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	141 / 358 (39.39%)		
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 358 (6.42%)		
occurrences (all)	23		
General disorders and administration site conditions			
Injection site Pain			
alternative assessment type: Systematic			
subjects affected / exposed	141 / 358 (39.39%)		
occurrences (all)	141		
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	25 / 358 (6.98%)		
occurrences (all)	25		
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 358 (7.26%)		
occurrences (all)	26		
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 358 (6.42%)		
occurrences (all)	23		
Malaise			
alternative assessment type: Systematic			
subjects affected / exposed	50 / 358 (13.97%)		
occurrences (all)	50		
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	52 / 358 (14.53%)		
occurrences (all)	52		

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