Clinical trial results:
Immunogenicity of Adacel® and BOOSTRIX® Vaccines in Adolescents

Summary

EudraCT number	2015-005629-38
Trial protocol	Outside EU/EEA
Global end of trial date	10 September 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	Td551

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01629589
WHO universal trial number (UTN)	U1111-1127-6774

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	1 Discovery Drive, Swiftwater, United States, 18370
Public contact	Medical Team Leader, Scientific and Medical Affairs Department, Sanofi Pasteur Inc., 1 570-957-5433, vitali.pool@sanofipasteur.com
Scientific contact	Medical Team Leader, Scientific and Medical Affairs Department, Sanofi Pasteur Inc., 1 570-957-5433, vitali.pool@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	08 May 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 September 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity
• To describe seroprotection rates against tetanus and diphtheria in subjects randomized to receive either Adacel or Boostrix vaccine.

• To describe pre- and post-vaccination tetanus, diphtheria, and pertussis geometric mean antibody concentrations (GMCs) in subjects randomized to receive either Adacel or Boostrix vaccine.

• To describe booster response rates against tetanus, diphtheria, and pertussis in subjects randomized to receive either Adacel or Boostrix vaccine.

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:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	20 June 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	United States: 423
Worldwide total number of subjects	423
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	423
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 20 June 2012 to 10 September 2012 at 8 centers in the United States.

Pre-assignment

Screening details:

A total of 423 subjects that met all of the inclusion and none of the exclusion criteria were randomized, 422 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	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Adacel® Vaccine Group

Arm description:

Subjects received a single dose of Adacel® 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 injection on Day 0.

Arm title	BOOSTRIX® Vaccine Group

Arm description:

Subjects received a single dose of BOOSTRIX® vaccine.

Arm type	Active comparator
Investigational medicinal product name	Tetanus toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine (BOOSTRIX®)
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 injection on Day 0.

Number of subjects in period 1	Adacel® Vaccine Group	BOOSTRIX® Vaccine Group
Started	212	211
Completed	204	204
Not completed	8	7
Consent withdrawn by subject	2	3
Did not receive study vaccine	-	1
Lost to follow-up	2	1
Protocol deviation	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Adacel® Vaccine Group
Reporting group description:	
Subjects received a single dose of Adacel® vaccine.	
Reporting group title	BOOSTRIX® Vaccine Group
Reporting group description:	
Subjects received a single dose of BOOSTRIX® vaccine.	

Reporting group values	Adacel® Vaccine Group	BOOSTRIX® Vaccine Group	Total
Number of subjects	212	211	423
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)	0	0	0
Adolescents (12-17 years)	212	211	423
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	11.6	11.6	
standard deviation	± 0.5	± 0.5	-
Gender categorical Units: Subjects			
Female	105	106	211
Male	107	105	212

End points

End points reporting groups

Reporting group title	Adacel® Vaccine Group
Reporting group description:	
Subjects received a single dose of Adacel® vaccine.	
Reporting group title	BOOSTRIX® Vaccine Group
Reporting group description:	
Subjects received a single dose of BOOSTRIX® vaccine.	

Primary: Number of Subjects With Antibody Responses to Tetanus and Diphtheria Components Following Vaccination With Either Adacel® or BOOSTRIX®

End point title	Number of Subjects With Antibody Responses to Tetanus and Diphtheria Components Following Vaccination With Either Adacel® or BOOSTRIX®[1]

End point description:

Tetanus antibody was assayed by enzyme-linked immunosorbent assay (ELISA) and Diphtheria antibody by a toxin neutralization test. Antibody responses to tetanus and diphtheria components were defined as titers ≥ 0.1 IU/mL and ≥ 1.0 IU/mL.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination) and 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® Vaccine Group	BOOSTRIX® Vaccine Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	194		
Units: Number of subjects				
number (not applicable)				
Tetanus (pre-vaccination); ≥ 0.1 IU/mL	172	177		
Tetanus (post-vaccination); ≥ 0.1 IU/mL	196	194		
Diphtheria (pre-vaccination); ≥ 0.1 IU/mL	135	139		
Diphtheria (post-vaccination); ≥ 0.1 IU/mL	196	194		
Tetanus (pre-vaccination); ≥ 1.0 IU/mL	33	48		
Tetanus (post-vaccination); ≥ 1.0 IU/mL	195	194		
Diphtheria (pre-vaccination); ≥ 1.0 IU/mL	28	26		
Diphtheria (post-vaccination); ≥ 1.0 IU/mL	183	186		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations of Tetanus and Diphtheria Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

End point title	Geometric Mean Concentrations of Tetanus and Diphtheria Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

End point description:

Tetanus antibody was assayed by enzyme-linked immunosorbent assay (ELISA) and Diphtheria antibody by a toxin neutralization test.

End point type	Secondary

End point timeframe:

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

End point values	Adacel® Vaccine Group	BOOSTRIX® Vaccine Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	194		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Tetanus (pre-vaccination)	0.422 (0.363 to 0.492)	0.456 (0.393 to 0.528)		
Tetanus (post-vaccination)	18.9 (16.4 to 21.8)	9.18 (8.1 to 10.4)		
Diphtheria (pre-vaccination)	0.211 (0.171 to 0.26)	0.221 (0.181 to 0.269)		
Diphtheria (post-vaccination)	8.17 (6.83 to 9.77)	5.62 (4.85 to 6.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Booster Responses Against Tetanus and Diphtheria Antigens Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

End point title	Number of Subjects With Booster Responses Against Tetanus and Diphtheria Antigens Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

End point description:

Adacel booster response defined as: a 4-fold increase in pre- to post-vaccination antibody concentrations for subjects with a pre-vaccination concentration ≤ 2.56 IU/mL for diphtheria and ≤ 2.7 IU/mL for tetanus, and defined as a 2-fold increase for subjects with a pre-vaccination concentration > 2.56 IU/mL for diphtheria and > 2.7 IU/mL for tetanus.

Boostrix booster response defined as: a post-vaccination titer ≥ 4 times the lower limit of quantitation (LLOQ) for subjects with a pre-vaccination titer < LLOQ, a post-vaccination titer ≥ 4 times the pre-vaccination titer for subjects with a pre-vaccination titer between LLOQ and 4X LLOQ, or a post-vaccination titer at least twice the pre-vaccination titer for subjects with a pre-vaccination titer ≥ 4X LLOQ.

End point type	Secondary

End point timeframe:

Day 28 post-vaccination

End point values	Adacel® Vaccine Group	BOOSTRIX® Vaccine Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	194		
Units: Number of subjects				
number (not applicable)				
Tetanus	194	191		
Diphtheria	189	188		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations of Pertussis Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

End point title	Geometric Mean Concentrations of Pertussis Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

End point description:

Pertussis antibodies Pertussis toxoid (PT), Filamentous hemagglutinin (FHA), Pertactin (PRN), and Fimbriae types 2 and 3 (FIM 2&3) were assayed by enzyme-linked immunosorbent assay (ELISA).

End point type	Secondary

End point timeframe:

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

End point values	Adacel® Vaccine Group	BOOSTRIX® Vaccine Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	194		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Pertussis toxoid (pre-vaccination)	5.59 (4.67 to 6.68)	5.69 (4.71 to 6.88)		
Pertussis toxoid (post-vaccination)	31 (27 to 35.7)	44.1 (39 to 49.9)		
Filamentous hemagglutinin (pre-vaccination)	22.7 (19 to 27.2)	22.7 (19.4 to 26.6)		
Filamentous hemagglutinin (post-vaccination)	255 (228 to 286)	318 (292 to 347)		
Pertactin (pre-vaccination)	12.3 (10.5 to 14.4)	10.3 (8.99 to 11.9)		
Pertactin (post-vaccination)	263 (223 to 310)	252 (214 to 295)		

Fimbriae types 2 and 3 (pre-vaccination)	5.95 (4.88 to 7.24)	6.55 (5.33 to 8.04)		
Fimbriae types 2 and 3 (post-vaccination)	346 (269 to 446)	11.1 (8.79 to 14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Booster Responses Against Pertussis Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

End point title	Number of Subjects With Booster Responses Against Pertussis Antibodies Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

End point description:

Adacel booster response defined as: a 4-fold increase in pre- to post-vaccination antibody concentrations for subjects with a pre-vaccination concentration ≤ 93 ELISA Unit (EU)/mL for Pertussis toxoid (PT), ≤ 170 EU/mL for Filamentous hemagglutinin (FHA), ≤ 115 EU/mL for pertactin (PRN), or ≤ 285 EU/mL for Fimbriae types 2 and 3 (FIM), and defined as a 2-fold increase for subjects with a pre-vaccination concentration > 93 EU/mL for PT, > 170 EU/mL for FHA, > 115 EU/mL for PRN, or > 285 EU/mL for FIM.

Boostrix booster response defined as: a post-vaccination titer ≥ 4 times the LLOQ for subjects with a pre-vaccination titer < LLOQ, a post-vaccination titer ≥ 4 times the pre-vaccination titer for subjects with a pre-vaccination titer between LLOQ and 4X LLOQ, or a post-vaccination titer at least twice the pre-vaccination titer for subjects with a pre-vaccination titer ≥ 4X LLOQ.

End point type	Secondary

End point timeframe:

Day 28 post-vaccination

End point values	Adacel® Vaccine Group	BOOSTRIX® Vaccine Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	194		
Units: Number of subjects				
number (not applicable)				
Pertussis toxoid	97	142		
Filamentous hemagglutinin	167	189		
Pertactin	186	189		
Fimbriae types 2 and 3	181	31		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Immediate Unsolicited Adverse Events Following Vaccination With Either Adacel® or BOOSTRIX® Vaccine

End point title	Number of Subjects Reporting Immediate Unsolicited Adverse Events Following Vaccination With Either Adacel® or

	BOOSTRIX® Vaccine

End point description:

The occurrence, nature (Medical Dictionary for Regulatory Activities [MedDRA] preferred term), duration, intensity, and relationship to vaccination of adverse events (AEs) reported in the 15 minutes after vaccination and systemic AEs.

End point type	Secondary

End point timeframe:

Up to 15 minutes post-vaccination

End point values	Adacel® Vaccine Group	BOOSTRIX® Vaccine Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	211		
Units: Number of subjects				
number (not applicable)				
Headache	1	0		
Nausea	1	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 Day 28 post-vaccination.	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0
Reporting groups	
Reporting group title	Adacel® Vaccine Group
Reporting group description:	
Subjects received a single dose of Adacel® vaccine.	
Reporting group title	BOOSTRIX® Vaccine Group
Reporting group description:	
Subjects received a single dose of BOOSTRIX® vaccine.	

Serious adverse events	Adacel® Vaccine Group	BOOSTRIX® Vaccine Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 211 (0.00%)	0 / 211 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Adacel® Vaccine Group	BOOSTRIX® Vaccine Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 211 (27.49%)	70 / 211 (33.18%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 211 (9.95%)	31 / 211 (14.69%)	
occurrences (all)	26	39	
General disorders and administration site conditions			
Injection site Pain			
alternative assessment type: Systematic			

subjects affected / exposed	34 / 211 (16.11%)	43 / 211 (20.38%)	
occurrences (all)	36	46	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 211 (5.21%)	4 / 211 (1.90%)	
occurrences (all)	11	5	

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