Clinical trial results:
Comparison of Pertussis Specific Cellular and Humoral Immunity Before and After a Acellular Pertussis Booster-Vaccination in Combination With a Diphtheria-Tetanus-Polio-Vaccine Between Three Groups of Adolescents 10-14 Years of Age That Have Previously Either Received 4 or 5 Doses of Acellular Pertussis Vaccine or 4 Doses of Whole-Cell Pertussis Vaccine

Summary

EudraCT number	2005-005532-27
Trial protocol	DE
Global end of trial date	31 October 2006

Results information

Result version number	v1 (current)
This version publication date	05 February 2016
First version publication date	27 March 2015

Trial information

Trial identification

Sponsor protocol code	PERTIMMUN06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur
Sponsor organisation address	1 Discovery Drive, Swiftwater, United States, 18370
Public contact	Vice President and Global Medical Expert, Sanofi Pasteur, +1 5709571506, Dr.Johnson@sanofipasteur.com
Scientific contact	Vice President and Global Medical Expert, Sanofi Pasteur, +1 5709571506, Dr.Johnson@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?	Yes
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 September 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 October 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the pertussis-specific humoral and cellular immunity after vaccination with REPEVAX® or COVAXiS® + IPV Merieux® among 3 groups:
Group A: Adolescents 10-14 years of age who had received five doses of acellular pertussis vaccine and who simultaneously participated in the TRI05 study in which they received either REPEVAX® or COVAXiS® + IPV Merieux® based on on their randomization group.
Group B: Adolescents 10-14 years of age who previously received four doses of acellular pertussis vaccine. Subjects of group B could not participate in the TRI05 study, and in this study received either REPEVAX® or COVAXiS® + IPV Merieux® as recommended by their physician.
Group C: Adolescents 10-14 years of age who previously received four doses of whole-cell pertussis vaccine and had not yet received acellular pertussis vaccine and who simultaneously participated in the TRI05 study in which they had received either REPEVAX® or COVAXiS® + IPV Merieux® based on their randomization group.

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 were also available on site in case of any immediate allergic reactions.

Background therapy:

Subjects may have received a 5th consecutive aP immunization at 4 - 6 years of age (which became part of the official German recommendations in March 2006) or have received only 4 consecutive aP or wP immunizations (last dose at 18-24 months).

Evidence for comparator:

Not applicable

Actual start date of recruitment	01 February 2006
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	Germany: 78
Worldwide total number of subjects	78
EEA total number of subjects	78

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)	22
Adolescents (12-17 years)	56
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 01 February 2006 to 16 August 2006 at 17 clinical centers in Germany.

Pre-assignment

Screening details:

A total of 78 subjects who met the inclusion, but none of the exclusion criteria were enrolled and vaccinated.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Study Group A

Arm description:

Adolescents 10 - 14 years of age, who had already been given 5 doses of an acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 4 to 6 years).

Arm type	Experimental
Investigational medicinal product name	REPEVAX
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

A single 0.5 ml dose

Investigational medicinal product name	COVAXiS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

A single 0.5 mL dose

Arm title	Study Group B

Arm description:

Adolescents 10-14 years of age, who had previously received 4 doses of acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 18 to 24 months).

Arm type	Experimental
Investigational medicinal product name	REPEVAX
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details: A single 0.5 ml dose	
Investigational medicinal product name	COVAXiS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: A single 0.5 mL dose	
Arm title	Study Group C
Arm description: Adolescents 10 - 14 years of age, who had already received 4 doses of whole-cell pertussis vaccine combined with diphtheria and tetanus toxoids (last at the age of 18 to 24 months) and who had so far not received an acellular pertussis vaccine.	
Arm type	Experimental
Investigational medicinal product name	REPEVAX
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: A single 0.5 ml dose	
Investigational medicinal product name	COVAXiS
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: A single 0.5 mL dose	

Number of subjects in period 1	Study Group A	Study Group B	Study Group C
Started	37	23	18
Completed	37	23	18

Baseline characteristics

Reporting groups	
Reporting group title	Study Group A
Reporting group description:	
Adolescents 10 - 14 years of age, who had already been given 5 doses of an acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 4 to 6 years).	
Reporting group title	Study Group B
Reporting group description:	
Adolescents 10-14 years of age, who had previously received 4 doses of acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 18 to 24 months).	
Reporting group title	Study Group C
Reporting group description:	
Adolescents 10 - 14 years of age, who had already received 4 doses of whole-cell pertussis vaccine combined with diphtheria and tetanus toxoids (last at the age of 18 to 24 months) and who had so far not received an acellular pertussis vaccine.	

Reporting group values	Study Group A	Study Group B	Study Group C
Number of subjects	37	23	18
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)	17	5	0
Adolescents (12-17 years)	20	18	18
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	12.2	12	13.3
standard deviation	± 0.2	± 0.5	± 0.3
Gender categorical Units: Subjects			
Female	15	12	6
Male	22	11	12

Reporting group values	Total		
Number of subjects	78		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		

Children (2-11 years)	22		
Adolescents (12-17 years)	56		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	33		
Male	45		

End points

End points reporting groups

Reporting group title	Study Group A
Reporting group description:	
Adolescents 10 - 14 years of age, who had already been given 5 doses of an acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 4 to 6 years).	
Reporting group title	Study Group B
Reporting group description:	
Adolescents 10-14 years of age, who had previously received 4 doses of acellular pertussis vaccine combined with diphtheria and tetanus toxoids (at that time Biken DTaP, last at the age of 18 to 24 months).	
Reporting group title	Study Group C
Reporting group description:	
Adolescents 10 - 14 years of age, who had already received 4 doses of whole-cell pertussis vaccine combined with diphtheria and tetanus toxoids (last at the age of 18 to 24 months) and who had so far not received an acellular pertussis vaccine.	

Primary: Summary of Geometric Mean Titers (GMTs) of Pertussis Antibodies Before and After a Acellular Pertussis Booster Vaccination

End point title	Summary of Geometric Mean Titers (GMTs) of Pertussis Antibodies Before and After a Acellular Pertussis Booster Vaccination[1]
End point description:	
End point type	Primary
End point timeframe:	
Day 0 (pre-vaccination) and 1 month 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 A	Study Group B	Study Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	23	18	
Units: EU/mL				
geometric mean (confidence interval 95%)				
IgG-Pertussis toxoid (pre-vaccination)	4.22 (3.24 to 5.48)	3.85 (2.83 to 5.25)	9.7 (4.18 to 22.47)	
IgG-Pertussis toxoid (post-vaccination)	16.35 (11.35 to 23.55)	17.06 (9.66 to 30.14)	50.33 (26.13 to 96.96)	
IgG-Filamentous hemagglutinin (pre-vaccination)	25.19 (16.78 to 37.82)	14.98 (9.39 to 23.9)	10.67 (5.21 to 21.89)	
igG-Filamentous hemagglutinin (post-vaccination)	160.97 (122.34 to 211.81)	127.04 (89.09 to 181.15)	135.57 (98.94 to 191.28)	
igG-Pertactin (pre-vaccination)	18.78 (12.5 to 28.21)	13.33 (6.34 to 28.02)	13.95 (6.3 to 30.87)	
igG-Pertactin (post-vaccination)	600.72 (449.61 to 802.63)	407.34 (260.6 to 636.7)	638.95 (370.02 to 1103.33)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with positive cell mediated immunity-response against Pertussis Toxoid (PT) Before and After Acellular Pertussis Booster Vaccination.

End point title	Percentage of Subjects with positive cell mediated immunity-response against Pertussis Toxoid (PT) Before and After Acellular Pertussis Booster Vaccination.

End point description:

A positive cell mediated immunity-response against PT is defined as a simulation index of ≥ 4.

End point type	Secondary

End point timeframe:

Pre-vaccination (Day 0) and Day 28 to 36 post-vaccination

End point values	Study Group A	Study Group B	Study Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	21	17	
Units: Percentage				
number (not applicable)				
Pre-vaccination	38	43	53	
Post-vaccination	62	81	77	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with positive Cell mediated immunity-response against Filamentous Hemagglutinin Before and After Acellular Pertussis Booster Vaccination.

End point title	Percentage of Subjects with positive Cell mediated immunity-response against Filamentous Hemagglutinin Before and After Acellular Pertussis Booster Vaccination.

End point description:

A positive cell mediated immunity-response against Filamentous Hemagglutinin was defined as a stimulation index (SI) of ≥4.

End point type	Secondary

End point timeframe:

Pre-vaccination (Day 0) and Day 28-36 Post-vaccination

End point values	Study Group A	Study Group B	Study Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	21	17	
Units: Percentage				
number (not applicable)				
Pre-vaccination	78	62	65	
Post-vaccination	87	95	94	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with positive Cell mediated immunity-response against Pertactin Before and After Acellular Pertussis Booster Vaccination.

End point title	Percentage of Subjects with positive Cell mediated immunity-response against Pertactin Before and After Acellular Pertussis Booster Vaccination.

End point description:

A positive cell mediated immunity-response against Pertactin was defined as a stimulation index (SI) of ≥4.

End point type	Secondary

End point timeframe:

Pre-vaccination (Day 0) and Day 28-36 Post-vaccination

End point values	Study Group A	Study Group B	Study Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	21	17	
Units: Percentage				
number (not applicable)				
Pre-vaccination	35	62	53	
Post-vaccination	68	71	82	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with positive Cell mediated immunity-response against Fimbriae type 2/3 Before and After Acellular Pertussis Booster Vaccination.

End point title	Percentage of Subjects with positive Cell mediated immunity-response against Fimbriae type 2/3 Before and After Acellular Pertussis Booster Vaccination.

End point description:

A positive cell mediated immunity-response against Fimbriae type 2/3 (FIM) was defined as a stimulation index (SI) of ≥4.

End point type	Secondary

End point timeframe:

Pre-vaccination (Day 0) and Day 28 to 36 Post-vaccination

End point values	Study Group A	Study Group B	Study Group C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	37	21	17	
Units: Percentage				
number (not applicable)				
Pre-vaccination	60	52	53	
Post-vaccination	73	76	82	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Safety outcomes including adverse events information were not part of this protocol and were not solicited during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	6.0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Safety outcomes including adverse events information were not part of this protocol and were not solicited during the study.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Not applicable

Notes: