



Clinical trial results:

Immune Response to Pertussis After Vaccination With a Tdap-IPV Booster Vaccine in Children in the Republic of South Africa: Effect of Homologous and Heterologous Pertussis Vaccination Priming Background

Summary

EudraCT number	2022-002452-40
Trial protocol	Outside EU/EEA
Global end of trial date	11 January 2023

Results information

Result version number	v1 (current)
This version publication date	15 October 2023
First version publication date	15 October 2023

Trial information

Trial identification

Sponsor protocol code	TD500056
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04300192
WHO universal trial number (UTN)	U1111-1223-5186

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur
Sponsor organisation address	14 Espace Henry Vallée, Lyon, France, 69007
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@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	12 July 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	11 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Humoral Immune Response: - To describe the long-term humoral immune responses to pertussis, diphtheria and tetanus after homologous and heterologous pertussis vaccine priming regimens.
- To determine the effects of the priming regimen on humoral responses to booster vaccination with tetanus toxoid, reduced diphtheria toxoid and acellular pertussis- inactivated poliomyelitis vaccine (Tdap-IPV) vaccine.

Cell-mediated Immunity: - To describe the long-term cell-mediated immune responses to pertussis after homologous and heterologous pertussis vaccine priming regimens. - To determine the effects of the priming regimen on cell-mediated immune response to booster vaccination with Tdap-IPV vaccine.

Protection of trial subjects:

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: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2021
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	South Africa: 274
Worldwide total number of subjects	274
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)	113
Adolescents (12-17 years)	161

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

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 3 active sites in South Africa from 27 January 2021 to 11 January 2023. Subjects primed with whole-cell pertussis (wP) and/or acellular pertussis (aP) vaccines in various combination as per national recommendation during their first 2 years of life were enrolled in this study

Pre-assignment

Screening details:

A total of 274 subjects were enrolled in the study, of which 1 subject was not assigned to any of the study groups and was not vaccinated due to determination of protocol deviation post-enrollment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Adacel Quadra® vaccine

Arm description:

Subjects primed with primary pertussis vaccination (4 doses of wP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as intramuscular (IM) injection on Day 0.

Arm type	Experimental
Investigational medicinal product name	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine
Investigational medicinal product code	
Other name	Adacel Quadra®, Repevax®, Triaxis® Polio, ADACEL®-POLIO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 millilitres (mL) IM injection into the deltoid muscle on Day 0.

Arm title	Group 2: Adacel Quadra® vaccine
------------------	---------------------------------

Arm description:

Subjects primed with primary pertussis vaccination (3 doses of wP vaccine followed by 1 dose of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Arm type	Experimental
Investigational medicinal product name	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine
Investigational medicinal product code	
Other name	Adacel Quadra®, Repevax®, Triaxis® Polio, ADACEL®-POLIO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL IM injection into the deltoid muscle on Day 0.

Arm title	Group 3: Adacel Quadra® vaccine
------------------	---------------------------------

Arm description:

Subjects primed with primary pertussis vaccination (2 doses of wP vaccine followed by 2 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Arm type	Experimental
Investigational medicinal product name	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine
Investigational medicinal product code	
Other name	Adacel Quadra®, Repevax®, Triaxis® Polio, ADACEL®-POLIO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: 0.5 mL IM injection into the deltoid muscle on Day 0.	
Arm title	Group 4: Adacel Quadra® vaccine

Arm description:

Subjects primed with primary pertussis vaccination (1 dose of wP vaccine followed by 3 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Arm type	Experimental
Investigational medicinal product name	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine
Investigational medicinal product code	
Other name	Adacel Quadra®, Repevax®, Triaxis® Polio, ADACEL®-POLIO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: 0.5 mL IM injection into the deltoid muscle on Day 0.	
Arm title	Group 5: Adacel Quadra® vaccine

Arm description:

Subjects primed with primary pertussis vaccination (4 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Arm type	Experimental
Investigational medicinal product name	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine
Investigational medicinal product code	
Other name	Adacel Quadra®, Repevax®, Triaxis® Polio, ADACEL®-POLIO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: 0.5 mL IM injection into the deltoid muscle on Day 0.	
Arm title	Group 6: Adacel Quadra® vaccine (HIV positive)

Arm description:

Subjects with human immunodeficiency virus (HIV) infection and primed with primary pertussis vaccination (4 doses of wP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Arm type	Experimental
Investigational medicinal product name	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine
Investigational medicinal product code	
Other name	Adacel Quadra®, Repevax®, Triaxis® Polio, ADACEL®-POLIO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL IM injection into the deltoid muscle on Day 0.

Arm title	Group 7: Adacel Quadra® vaccine (HIV positive)
Arm description: Subjects with HIV infection and primed with primary pertussis vaccination (4 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Arm type	Experimental
Investigational medicinal product name	Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliomyelitis Vaccine
Investigational medicinal product code	
Other name	Adacel Quadra®, Repevax®, Triaxis® Polio, ADACEL®-POLIO
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: 0.5 mL IM injection into the deltoid muscle on Day 0.	

Number of subjects in period 1^[1]	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine
Started	103	29	4
Vaccinated	103	29	4
Completed	103	29	4
Not completed	0	0	0
Protocol deviation	-	-	-

Number of subjects in period 1^[1]	Group 4: Adacel Quadra® vaccine	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)
Started	1	103	10
Vaccinated	1	102	10
Completed	1	102	7
Not completed	0	1	3
Protocol deviation	-	1	3

Number of subjects in period 1^[1]	Group 7: Adacel Quadra® vaccine (HIV positive)
Started	23
Vaccinated	22
Completed	18
Not completed	5
Protocol deviation	5

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One subject was not assigned to any of the study groups and was not vaccinated due to determination of protocol deviation post-enrollment.

Baseline characteristics

Reporting groups

Reporting group title	Group 1: Adacel Quadra® vaccine
Reporting group description:	
Subjects primed with primary pertussis vaccination (4 doses of wP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as intramuscular (IM) injection on Day 0.	
Reporting group title	Group 2: Adacel Quadra® vaccine
Reporting group description:	
Subjects primed with primary pertussis vaccination (3 doses of wP vaccine followed by 1 dose of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 3: Adacel Quadra® vaccine
Reporting group description:	
Subjects primed with primary pertussis vaccination (2 doses of wP vaccine followed by 2 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 4: Adacel Quadra® vaccine
Reporting group description:	
Subjects primed with primary pertussis vaccination (1 dose of wP vaccine followed by 3 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 5: Adacel Quadra® vaccine
Reporting group description:	
Subjects primed with primary pertussis vaccination (4 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 6: Adacel Quadra® vaccine (HIV positive)
Reporting group description:	
Subjects with human immunodeficiency virus (HIV) infection and primed with primary pertussis vaccination (4 doses of wP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 7: Adacel Quadra® vaccine (HIV positive)
Reporting group description:	
Subjects with HIV infection and primed with primary pertussis vaccination (4 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	

Reporting group values	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine
Number of subjects	103	29	4
Age categorical			
Units: Subjects			
Age continuous			
Here, '99999' was used as a space filler which denotes that standard deviation (SD) was not calculable because only one subject was involved in the analysis.			
Units: years			
arithmetic mean	14.0	12.5	12.0
standard deviation	± 0.685	± 0.509	± 0
Gender categorical			
Units: Subjects			
Female	60	10	2
Male	43	19	2

Reporting group values	Group 4: Adacel Quadra® vaccine	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)
Number of subjects	1	103	10
Age categorical Units: Subjects			

Age continuous			
Here, '99999' was used as a space filler which denotes that standard deviation (SD) was not calculable because only one subject was involved in the analysis.			
Units: years arithmetic mean standard deviation	12.0 ± 99999	10.4 ± 0.803	13.2 ± 1.32
Gender categorical Units: Subjects			
Female	0	50	2
Male	1	53	8

Reporting group values	Group 7: Adacel Quadra® vaccine (HIV positive)	Total	
Number of subjects	23	273	
Age categorical Units: Subjects			

Age continuous			
Here, '99999' was used as a space filler which denotes that standard deviation (SD) was not calculable because only one subject was involved in the analysis.			
Units: years arithmetic mean standard deviation	10.8 ± 0.984	-	
Gender categorical Units: Subjects			
Female	10	134	
Male	13	139	

End points

End points reporting groups

Reporting group title	Group 1: Adacel Quadra® vaccine
Reporting group description: Subjects primed with primary pertussis vaccination (4 doses of wP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as intramuscular (IM) injection on Day 0.	
Reporting group title	Group 2: Adacel Quadra® vaccine
Reporting group description: Subjects primed with primary pertussis vaccination (3 doses of wP vaccine followed by 1 dose of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 3: Adacel Quadra® vaccine
Reporting group description: Subjects primed with primary pertussis vaccination (2 doses of wP vaccine followed by 2 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 4: Adacel Quadra® vaccine
Reporting group description: Subjects primed with primary pertussis vaccination (1 dose of wP vaccine followed by 3 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 5: Adacel Quadra® vaccine
Reporting group description: Subjects primed with primary pertussis vaccination (4 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 6: Adacel Quadra® vaccine (HIV positive)
Reporting group description: Subjects with human immunodeficiency virus (HIV) infection and primed with primary pertussis vaccination (4 doses of wP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	
Reporting group title	Group 7: Adacel Quadra® vaccine (HIV positive)
Reporting group description: Subjects with HIV infection and primed with primary pertussis vaccination (4 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.	

Primary: Geometric Mean Concentrations (GMCs) of Total Immunoglobulin G (IgG) Anti-pertussis Antibodies Against Pertussis Antigens

End point title	Geometric Mean Concentrations (GMCs) of Total Immunoglobulin G (IgG) Anti-pertussis Antibodies Against Pertussis Antigens ^[1]
End point description: GMCs of IgG anti-pertussis antibodies: anti-pertussis (anti-PT) toxin, anti-filamentous hemagglutinin (anti-FHA), anti-pertactin (anti-PRN) and anti-fimbriae (anti-FIM) types 2 and 3 were measured by multiplexed meso scale discovery electrochemiluminescence (MSD ECL) assay. Results were expressed in enzyme-linked immunosorbent assay (ELISA) units (EU)/mL. Analysis was performed on full analysis set (FAS) which included subjects who received a dose of the study vaccine and with pre-vaccination or post-vaccination blood sample results available. Here, '-99999 and 99999' were used as a space filler which denotes that 95 percent (%) confidence interval (CI) was not computable due to the low number of subjects.	
End point type	Primary
End point timeframe: Day 0 (pre-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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine	Group 4: Adacel Quadra® vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	103	29	4	1
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PT IgG	9.13 (6.96 to 12.0)	9.01 (6.03 to 13.5)	10.9 (-99999 to 99999)	11.3 (-99999 to 99999)
Anti-FHA IgG	48.0 (38.8 to 59.2)	37.1 (26.2 to 52.5)	39.7 (-99999 to 99999)	23.7 (-99999 to 99999)
Anti-PRN IgG	7.63 (5.83 to 10.0)	2.81 (1.88 to 4.22)	3.98 (-99999 to 99999)	1.00 (-99999 to 99999)
Anti-FIM 2 & 3 IgG	38.7 (30.5 to 49.1)	15.1 (9.00 to 25.2)	9.33 (-99999 to 99999)	7.48 (-99999 to 99999)

End point values	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)	Group 7: Adacel Quadra® vaccine (HIV positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	10	22	
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PT IgG	7.08 (5.76 to 8.71)	12.1 (5.83 to 25.0)	26.5 (17.2 to 40.8)	
Anti-FHA IgG	42.5 (35.8 to 50.4)	52.3 (25.3 to 108)	104 (63.4 to 170)	
Anti-PRN IgG	1.65 (1.41 to 1.93)	4.46 (1.86 to 10.7)	3.36 (2.05 to 5.50)	
Anti-FIM 2 & 3 IgG	2.11 (1.71 to 2.60)	13.0 (3.68 to 46.0)	1.83 (1.10 to 3.03)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations of Total Immunoglobulin G Anti-pertussis Antibodies Against Pertussis Antigens

End point title	Geometric Mean Concentrations of Total Immunoglobulin G Anti-pertussis Antibodies Against Pertussis Antigens ^[2]
-----------------	-----------------------------------------------------------------------------------------------------------------------------

End point description:

GMCs of IgG anti-pertussis antibodies: anti-PT toxin, anti-FHA, anti-PRN and anti-FIM types 2 and 3 were measured by multiplexed MSD ECL assay. Results were expressed in EU/mL. Analysis was

performed on FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint and '-99999 and 99999' were used as a space filler which denotes that 95% CI was not computable due to the low number of subjects.

End point type	Primary
End point timeframe:	
Day 30 (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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine	Group 4: Adacel Quadra® vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	101	29	4	1
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PT IgG	102 (82.9 to 124)	141 (107 to 187)	142 (-99999 to 99999)	110 (-99999 to 99999)
Anti-FHA IgG	410 (351 to 479)	379 (306 to 470)	233 (-99999 to 99999)	199 (-99999 to 99999)
Anti-PRN IgG	484 (370 to 632)	250 (174 to 361)	410 (-99999 to 99999)	438 (-99999 to 99999)
Anti-FIM 2 & 3 IgG	2097 (1750 to 2513)	1039 (648 to 1664)	1542 (-99999 to 99999)	1133 (-99999 to 99999)

End point values	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)	Group 7: Adacel Quadra® vaccine (HIV positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	10	22	
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PT IgG	117 (98.1 to 138)	117 (49.7 to 276)	148 (108 to 201)	
Anti-FHA IgG	366 (318 to 422)	439 (239 to 806)	549 (387 to 779)	
Anti-PRN IgG	74.0 (50.4 to 109)	174 (52.3 to 577)	87.1 (36.5 to 208)	
Anti-FIM 2 & 3 IgG	168 (117 to 242)	1226 (527 to 2853)	78.9 (39.6 to 157)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations of Total Immunoglobulin G Anti-diphtheria

Antibodies

End point title	Geometric Mean Concentrations of Total Immunoglobulin G Anti-diphtheria Antibodies ^[3]
-----------------	---------------------------------------------------------------------------------------------------

End point description:

GMCs of IgG anti-diphtheria antibodies were measured by multiplexed MSD ECL assay. Results were expressed in international units per millilitre (IU/mL). Analysis was performed on FAS. Here, '-99999 and 99999' were used as a space filler which denotes that 95% CI was not computable due to the low number of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 0 (pre-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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine	Group 4: Adacel Quadra® vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	103	29	4	1
Units: IU/mL				
geometric mean (confidence interval 95%)	0.104 (0.075 to 0.147)	0.123 (0.056 to 0.271)	0.432 (-99999 to 99999)	0.050 (-99999 to 99999)

End point values	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)	Group 7: Adacel Quadra® vaccine (HIV positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	10	22	
Units: IU/mL				
geometric mean (confidence interval 95%)	0.279 (0.202 to 0.386)	0.039 (0.009 to 0.174)	0.103 (0.036 to 0.298)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations of Total Immunoglobulin G Anti-diphtheria Antibodies

End point title	Geometric Mean Concentrations of Total Immunoglobulin G Anti-diphtheria Antibodies ^[4]
-----------------	---------------------------------------------------------------------------------------------------

End point description:

GMCs of IgG anti-diphtheria antibodies were measured by multiplexed MSD ECL assay. Results were expressed in IU/mL. Analysis was performed on FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint; and '-99999 and 99999' were used as a space filler which denotes that 95% CI was not computable due to the low number of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 30 (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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine	Group 4: Adacel Quadra® vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	101	29	4	1
Units: IU/mL				
geometric mean (confidence interval 95%)	2.03 (1.69 to 2.44)	2.06 (1.48 to 2.89)	3.79 (-99999 to 99999)	6.49 (-99999 to 99999)

End point values	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)	Group 7: Adacel Quadra® vaccine (HIV positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	10	22	
Units: IU/mL				
geometric mean (confidence interval 95%)	4.79 (4.03 to 5.68)	0.913 (0.206 to 4.04)	2.49 (1.44 to 4.32)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations of Total Immunoglobulin G Anti-tetanus Antibodies

End point title	Geometric Mean Concentrations of Total Immunoglobulin G Anti-tetanus Antibodies ^[5]
-----------------	------------------------------------------------------------------------------------------------

End point description:

GMCs of IgG anti-tetanus antibodies were measured by multiplexed MSD ECL assay. Results were expressed in IU/mL. Analysis was performed on FAS. Here, '-99999 and 99999' were used as a space filler which denotes that 95% CI was not computable due to the low number of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 0 (pre-vaccination)

Notes:

[5] - 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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine	Group 4: Adacel Quadra® vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	103	29	4	1
Units: IU/mL				
geometric mean (confidence interval 95%)	0.706 (0.483 to 1.03)	1.51 (0.716 to 3.17)	2.38 (-99999 to 99999)	0.040 (-99999 to 99999)

End point values	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)	Group 7: Adacel Quadra® vaccine (HIV positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	10	22	
Units: IU/mL				
geometric mean (confidence interval 95%)	0.528 (0.374 to 0.746)	0.112 (0.025 to 0.494)	0.319 (0.126 to 0.809)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentrations of Total Immunoglobulin G Anti-tetanus Antibodies

End point title	Geometric Mean Concentrations of Total Immunoglobulin G Anti-tetanus Antibodies ^[6]
-----------------	------------------------------------------------------------------------------------------------

End point description:

GMCs of IgG anti-tetanus antibodies were measured by multiplexed MSD ECL assay. Results were expressed in IU/mL. Analysis was performed on FAS. Here, 'number of subjects analysed' = subjects with available data for this endpoint; and '-99999 and 99999' were used as a space filler which denotes that 95% CI was not computable due to the low number of subjects.

End point type	Primary
----------------	---------

End point timeframe:

Day 30 (post-vaccination)

Notes:

[6] - 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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine	Group 4: Adacel Quadra® vaccine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	101	29	4	1
Units: IU/mL				
geometric mean (confidence interval 95%)	14.8 (12.8 to 17.2)	13.7 (10.3 to 18.2)	11.5 (-99999 to 99999)	13.3 (-99999 to 99999)

End point values	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)	Group 7: Adacel Quadra® vaccine (HIV positive)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	10	22	
Units: IU/mL				
geometric mean (confidence interval 95%)	9.99 (8.58 to 11.6)	9.69 (3.91 to 24.0)	8.65 (5.08 to 14.7)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited adverse event (AE) data were collected from Day 0 up to 30 days after vaccination. Solicited reactions data were collected within 7 days after vaccination. Serious adverse events data were collected throughout the study (i.e., up to Day 30)

Adverse event reporting additional description:

Analysis was performed on safety analysis set which included all subjects who received the study vaccine and had any safety data available.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	23.1
--------------------	------

Reporting groups

Reporting group title	Group 1: Adacel Quadra® vaccine
-----------------------	---------------------------------

Reporting group description:

Subjects primed with primary pertussis vaccination (4 doses of wP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Reporting group title	Group 2: Adacel Quadra® vaccine
-----------------------	---------------------------------

Reporting group description:

Subjects primed with primary pertussis vaccination (3 doses of wP vaccine followed by 1 dose of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Reporting group title	Group 3: Adacel Quadra® vaccine
-----------------------	---------------------------------

Reporting group description:

Subjects primed with primary pertussis vaccination (2 doses of wP vaccine followed by 2 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Reporting group title	Group 4: Adacel Quadra® vaccine
-----------------------	---------------------------------

Reporting group description:

Subjects primed with primary pertussis vaccination (1 dose of wP vaccine followed by 3 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Reporting group title	Group 5: Adacel Quadra® vaccine
-----------------------	---------------------------------

Reporting group description:

Subjects primed with primary pertussis vaccination (4 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Reporting group title	Group 6: Adacel Quadra® vaccine (HIV positive)
-----------------------	------------------------------------------------

Reporting group description:

Subjects with HIV infection and primed with primary pertussis vaccination (4 doses of wP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Reporting group title	Group 7: Adacel Quadra® vaccine (HIV positive)
-----------------------	------------------------------------------------

Reporting group description:

Subjects with HIV infection and primed with primary pertussis vaccination (4 doses of aP vaccine during first 2 years of life) received a single dose of Adacel Quadra® vaccine as IM injection on Day 0.

Serious adverse events	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 103 (0.00%)	0 / 29 (0.00%)	0 / 4 (0.00%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Group 4: Adacel Quadra® vaccine	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 102 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Group 7: Adacel Quadra® vaccine (HIV positive)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Group 1: Adacel Quadra® vaccine	Group 2: Adacel Quadra® vaccine	Group 3: Adacel Quadra® vaccine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 103 (85.44%)	20 / 29 (68.97%)	3 / 4 (75.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	43 / 103 (41.75%)	6 / 29 (20.69%)	3 / 4 (75.00%)
occurrences (all)	45	6	3
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	23 / 103 (22.33%)	3 / 29 (10.34%)	0 / 4 (0.00%)
occurrences (all)	23	3	0
Injection Site Pain			
subjects affected / exposed	74 / 103 (71.84%)	18 / 29 (62.07%)	3 / 4 (75.00%)
occurrences (all)	74	18	3
Injection Site Swelling			

subjects affected / exposed occurrences (all)	29 / 103 (28.16%) 29	9 / 29 (31.03%) 9	0 / 4 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	31 / 103 (30.10%) 31	1 / 29 (3.45%) 1	0 / 4 (0.00%) 0
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all)	1 / 103 (0.97%) 1	2 / 29 (6.90%) 2	0 / 4 (0.00%) 0
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	25 / 103 (24.27%) 25	1 / 29 (3.45%) 1	0 / 4 (0.00%) 0
Infections and infestations Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	4 / 103 (3.88%) 4	0 / 29 (0.00%) 0	0 / 4 (0.00%) 0

Non-serious adverse events	Group 4: Adacel Quadra® vaccine	Group 5: Adacel Quadra® vaccine	Group 6: Adacel Quadra® vaccine (HIV positive)
Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 1 (100.00%)	71 / 102 (69.61%)	8 / 10 (80.00%)
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1	23 / 102 (22.55%) 24	4 / 10 (40.00%) 4
General disorders and administration site conditions Injection Site Erythema subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	13 / 102 (12.75%) 13	2 / 10 (20.00%) 2
Injection Site Pain subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	62 / 102 (60.78%) 62	5 / 10 (50.00%) 5
Injection Site Swelling subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	27 / 102 (26.47%) 27	3 / 10 (30.00%) 3
Malaise			

subjects affected / exposed occurrences (all)	1 / 1 (100.00%) 1	5 / 102 (4.90%) 5	1 / 10 (10.00%) 1
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 102 (0.98%) 1	0 / 10 (0.00%) 0
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 102 (0.98%) 1	1 / 10 (10.00%) 1
Infections and infestations Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	6 / 102 (5.88%) 6	1 / 10 (10.00%) 1

Non-serious adverse events	Group 7: Adacel Quadra® vaccine (HIV positive)		
Total subjects affected by non-serious adverse events subjects affected / exposed	21 / 22 (95.45%)		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4		
General disorders and administration site conditions Injection Site Erythema subjects affected / exposed occurrences (all) Injection Site Pain subjects affected / exposed occurrences (all) Injection Site Swelling subjects affected / exposed occurrences (all) Malaise subjects affected / exposed occurrences (all)	5 / 22 (22.73%) 5 17 / 22 (77.27%) 17 11 / 22 (50.00%) 11 6 / 22 (27.27%) 6		
Gastrointestinal disorders			

Abdominal Pain subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 3		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3		
Infections and infestations Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2019	Following changes were made: The word 'minutes' was added as per EC's comment; Added statement: "The parents or their child may withdraw their consent to the storage of samples at any time during the study. If at the age of 18, the child decides to withdraw his/her consent for the storage of his/her samples, he/she will have to contact the site who will inform the sponsor of the study to destroy his/her samples."; throughout the study the age of subject was changed from 8 through 12 years to 9 through 13 years; To align to Art 46 of Regulation (EC) No 1901/2006 for pediatric studies and also to the public disclosure of the study results modalities, the study results should be submitted no later than 6 months after the last visit of last subject (LVLS). As the cell-mediated immunity (CMI) results would be available later than 6 months after the LVLS, it was decided to release a first CSR with available data 6 months after the LVLS and the final clinical study report (CSR) when the CMI results are available; Text was updated to reflect that there was no coordinating investigator but there was a principal investigator; Planned study timelines were updated; Updated the exclusion criteria text to reflect: If the subject has a primary physician who is not the Investigator, the site must obtain the subject's / subject's parent or legal guardian's consent prior to contacting this physician and informing him/her of the subject's participation in the study; Updated text to reflect: All statistical analyses will be performed under the responsibility of the Sponsor's Biostatistics Platform using the SAS® software, Version 9.4 or newer (SAS Institute, Cary, North Carolina, USA); Updated table of study procedures.
14 October 2020	Following changes were made: The cover page was updated with details of the new regional trial manager; Number of subjects was corrected throughout; Corrected and clarified the synopsis and immunogenicity endpoints; Updated identity of study product; Updated visit procedures; Updated planned study calendar; Updated randomisation and allocation procedures to provide clarification of subject number; Updated blood samples for CMI; Clarified sample storage and shipment to Global Clinical Immunology (GCI); Corrected sample storage and shipment to research-Eu Marcy l'Etoile, France; Corrected future use of stored serum samples for research; Updated immunogenicity assessment method. Updated the cover page to replace the age of subjects by the years of birth, updated details of the new medical study leader and global safety office; Updated synopsis, study design, schedule of study procedures and methodology; Updated inclusion and exclusion criteria; Updated background section, recruitment procedures, identity of study product; timelines in the planned study calendar section were updated.
18 October 2022	Following changes were made: Updated title page to reflect changes within the company; Replaced 'subject' with 'participant', 'trial' with 'study' and Research-EU Human Immunology Platform was replaced by Vaccine R&D, Clinical Exploratory Research Platform throughout the document; Clarified regarding the number of subjects concerned by blood sampling for the humoral immune response; Updated the study calendar; Clarified on the HIV treatment medications; Updated the immunogenicity endpoints due to the development of a more sensitive assay; The exploratory assay for the quantification of the memory B cells by Fluorospot was suppressed because of the difficult interpretation of the results for IgM and IgA secreting cells. The dual color Fluorospot was replaced by a more sensitive triple Fluorospot to measure interferon (IFN)- γ , Interleukin (IL)-17, and IL-4 to interrogate the Th profile. The Luminex assay on culture supernatant was also suppressed as this assay is redundant and less sensitive than the Fluorospot assay.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported