# 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 |
| 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 | 12.0 | 10.4 | 13.2 |
| standard deviation | ± 99999 | ± 0.803 | ± 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 | 10.8 | | |
| standard deviation | ± 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-diphteria

## Antibodies

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

End point description:

GMCs of IgG anti-diphteria 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-diphteria Antibodies

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

End point description:

GMCs of IgG anti-diphteria 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 | 29 / 103 (28.16%) | 9 / 29 (31.03%) | 0 / 4 (0.00%) |
| occurrences (all) | 29 | 9 | 0 |
| Malaise | | | |
| subjects affected / exposed | 31 / 103 (30.10%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences (all) | 31 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 1 / 103 (0.97%) | 2 / 29 (6.90%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 25 / 103 (24.27%) | 1 / 29 (3.45%) | 0 / 4 (0.00%) |
| occurrences (all) | 25 | 1 | 0 |
| Infections and infestations | | | |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 4 / 103 (3.88%) | 0 / 29 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 4 | 0 | 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 | 1 / 1 (100.00%) | 23 / 102 (22.55%) | 4 / 10 (40.00%) |
| occurrences (all) | 1 | 24 | 4 |
| General disorders and administration site conditions | | | |
| Injection Site Erythema | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 13 / 102 (12.75%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 13 | 2 |
| Injection Site Pain | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 62 / 102 (60.78%) | 5 / 10 (50.00%) |
| occurrences (all) | 0 | 62 | 5 |
| Injection Site Swelling | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 27 / 102 (26.47%) | 3 / 10 (30.00%) |
| occurrences (all) | 0 | 27 | 3 |
| Malaise | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 1 (100.00%) | 5 / 102 (4.90%) | 1 / 10 (10.00%) |
| occurrences (all) | 1 | 5 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 102 (0.98%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 102 (0.98%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Infections and infestations | | | |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 6 / 102 (5.88%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 6 | 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 | 4 / 22 (18.18%) | | |
| occurrences (all) | 4 | | |
| General disorders and administration site conditions | | | |
| Injection Site Erythema | | | |
| subjects affected / exposed | 5 / 22 (22.73%) | | |
| occurrences (all) | 5 | | |
| Injection Site Pain | | | |
| subjects affected / exposed | 17 / 22 (77.27%) | | |
| occurrences (all) | 17 | | |
| Injection Site Swelling | | | |
| subjects affected / exposed | 11 / 22 (50.00%) | | |
| occurrences (all) | 11 | | |
| Malaise | | | |
| subjects affected / exposed | 6 / 22 (27.27%) | | |
| occurrences (all) | 6 | | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Abdominal Pain<br>subjects affected / exposed<br>occurrences (all) | 2 / 22 (9.09%)<br>3 | | |
| Musculoskeletal and connective tissue disorders<br>Myalgia<br>subjects affected / exposed<br>occurrences (all) | 3 / 22 (13.64%)<br>3 | | |
| Infections and infestations<br>Upper Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all) | 4 / 22 (18.18%)<br>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 calender; 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 calender; 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