# Clinical trial results:
# A Phase II/III, Multicenter, Randomized, Observer-blinded, Active Controlled Clinical Study to Assess the Safety and Immunogenicity of the Tetanus, Diphtheria and Acellular Pertussis Vaccine SIIPL Tdap in Comparison with Boostrix® in Healthy Adults, Adolescents and Children

## Summary

| | |
|---|---|
| EudraCT number | 2019-002706-46 |
| Trial protocol | DE |
| Global end of trial date | 14 June 2021 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 15 December 2022 |
| First version publication date | 15 December 2022 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | DE-3.01_SII-Tdap |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Vakzine Projekt Management GmbH |
| Sponsor organisation address | Mellendorfer Str. 9 , Hannover, Germany, 30625 |
| Public contact | CT Tdap Info, Vakzine Projekt Management GmbH, +49 511169908 0, info@vakzine-manager.de |
| Scientific contact | CT Tdap Info, Vakzine Projekt Management GmbH, +49 511169908 0, info@vakzine-manager.de |

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? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 07 January 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 14 June 2021 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Phase II: To assess the reactogenicity and safety of a single dose of SIIPL (Serum Institute of India Pvt. Ltd) Tdap (tetanus, diphtheria and acellular pertussis) in comparison with a single dose of Boostrix® in healthy subjects of age 18 to 65 years.

Phase III: To demonstrate non-inferiority of SIIPL Tdap with a margin of 10% compared to Boostrix® in terms of seroprotection rates against diphtheria and tetanus 30 days after vaccination, in healthy subjects of age 4 to 65 years. To demonstrate non-inferiority of SIIPL Tdap with a margin of 10% compared to Boostrix® in terms of booster response to pertussis toxoid (PT), filamentous hemagglutinin (FHA) and pertactin (PRN), 30 days after vaccination, in healthy subjects of age 4 to 65 years.

Protection of trial subjects:

At each study center, the protocol and informed consent form (ICF) for this study were reviewed and approved by a duly constituted Institutional Review Board (IRB) or Independent Ethics Committee (IEC) and provided to the Contract Research Organization (CRO) before subjects were screened for entry. A letter documenting the IRB/IEC approval was provided to the CRO prior to initiation of the study. Amendments to the protocol were reviewed and approved in the same manner before being implemented.
This study was designed and monitored in accordance with the CRO’s standard operating procedures (SOPs), which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki as amended by the 64th World Medical Association (WMA) General Assembly in October 2013 and the Council for International Organizations of Medical Sciences International Ethical Guidelines, as well as for any local applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 26 February 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Germany: 1334 |
| Worldwide total number of subjects | 1334 |
| EEA total number of subjects | 1334 |

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) | 75 |
| Adolescents (12-17 years) | 75 |
| Adults (18-64 years) | 1176 |
| From 65 to 84 years | 8 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 14 centers in Germany from 26Feb20 to 14Jun21 [randomized 1334 subjects]. The study was performed in 2 phases: Phase II and III. The following age cohorts were: Phase II and III Cohort 1 – Adults from 18 to 65 years; Phase III Cohort 2 – Adolescents from 12 to 17 years;  Phase III Cohort 3 – Children from 4 to 11 years.

### Pre-assignment

Screening details:

The screening period was of 1 day. All the study assessments were performed as per the schedule of assessment. The study conduct was almost identical in Phase II and Phase III parts of the study. Subjects were randomized in a ratio of 2:1 (SIIPL Tdap: Boostrix®).

### Period 1

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

Blinding implementation details:

To ensure blinding of the assessment of safety and reactogenicity after vaccine administration, unblinded site staff were used for vaccine administration and blinded site staff were used for safety and reactogenicity assessment. The subjects, the investigator evaluating the subject, the clinical staff evaluating the subject, and the Sponsor personnel were blinded to treatment allocation.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | SIIPL Tdap |

Arm description:

Subjects received SIIPL Tdap vaccine in phase II and  Phase III period.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | SIIPL Tdap |
| Investigational medicinal product code | |
| Other name | Tdap vaccine |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single dose (0.5 ml) of SIIPL vaccine via deep intramuscular injection.

| | |
|---|---|
| **Arm title** | Boostrix® |

Arm description:

Subjects received the Boostrix® vaccine in phase II and Phase III periods.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Boostrix® |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single dose (0.5 ml) of Boostrix® via deep intramuscular injection.

| **Number of subjects in period 1[1]** | SIIPL Tdap | Boostrix® |
|---|---|---|
| Started | 887 | 445 |
| Completed | 884 | 445 |
| Not completed | 3 | 0 |
| Consent withdrawn by subject | 1 | - |
| Lost to follow-up | 2 | - |

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: Two subjects randomized, not treated and discontinued. Two subjects were excluded in the subject disposition table.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | SIIPL Tdap |
| Reporting group description: | |
| Subjects received SIIPL Tdap vaccine in phase II and Phase III period. | |
| Reporting group title | Boostrix® |
| Reporting group description: | |
| Subjects received the Boostrix® vaccine in phase II and Phase III periods. | |

| Reporting group values | SIIPL Tdap | Boostrix® | Total |
|---|---|---|---|
| Number of subjects | 887 | 445 | 1332 |
| Age categorical<br>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) | 50 | 25 | 75 |
| Adolescents (12-17 years) | 50 | 25 | 75 |
| Adults (18-64 years) | 783 | 391 | 1174 |
| From 65-84 years | 4 | 4 | 8 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 37.9 | 37.5 | |
| standard deviation | ± 15.83 | ± 16.0 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 462 | 221 | 683 |
| Male | 425 | 224 | 649 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | SIIPL Tdap |
| Reporting group description: | |
| Subjects received SIIPL Tdap vaccine in phase II and Phase III period. | |
| Reporting group title | Boostrix® |
| Reporting group description: | |
| Subjects received the Boostrix® vaccine in phase II and Phase III periods. | |

### Primary: Numbers of subjects with Adverse events (AE) and serious AEs (SAEs)

| | |
|---|---|
| End point title | Numbers of subjects with Adverse events (AE) and serious AEs (SAEs)[1] |

End point description:

The reactogenicity and safety of a single dose of SIIPL Tdap in comparison with a single dose of Boostrix® in healthy subjects were assesed .
The overall AEs were reported as solicited AEs at 30 minutes post-injection, from Day 0 to Day 6, and those continuing beyond Day 6 (recorded as unsolicited AEs and Unsolicited treatment-emergent AEs (i.e., excluding solicited AEs).
All screened subjects who provided informed consent, were enrolled, and vaccinated. Subjects were analyzed based on the actual treatment received at Visit 1 (Day 0). Those treated subjects were expected to provide data for safety analyses.

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

End point timeframe:

30 minutes post injection, Day 0 to day 6 and beyond Day 6 to 30

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: Statistical data is not available for this primary endpoint.

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 887 | 445 | | |
| Units: subjects | | | | |
| Any Solicited AE (post 30 min) | 14 | 7 | | |
| Local Solicited AEs (post 30 min) | 7 | 2 | | |
| Systemic Solicited AEs (post 30 min) | 7 | 5 | | |
| Any drug related serious AE (post 30 min) | 0 | 0 | | |
| Any AE leading to death (post 30 min) | 0 | 0 | | |
| Any Solicited AE (Day 0-6) | 653 | 335 | | |
| Local Solicited AEs (Day 0-6) | 580 | 289 | | |
| Systemic Solicited AEs (Day 0-6) | 414 | 197 | | |
| Any drug related serious AE (Day 0-6) | 0 | 0 | | |
| Any AE leading to death (Day 0-6) | 0 | 0 | | |
| Any AE (beyond Day 6) | 43 | 13 | | |
| Any drug related AE (beyond Day 6) | 40 | 11 | | |
| Any serious AE (beyond Day 6) | 0 | 0 | | |
| Any drug related serious AE (beyond Day 6) | 0 | 0 | | |
| Any AE leading to death (beyond Day 6) | 0 | 0 | | |

| | | | | |
|---|---|---|---|---|
| Any Unsolicited AE | 310 | 128 | | |
| Any drug related Unsolicited AE | 113 | 42 | | |
| Any serious Unsolicited AE | 3 | 1 | | |
| Any drug related serious Unsolicited AE | 0 | 0 | | |
| Any Unsolicited AE leading to death | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Seroprotection rate against Diphtheria Toxoid (DT)

| | |
|---|---|
| End point title | Seroprotection rate against Diphtheria Toxoid (DT) |

End point description:

The non-inferiority of SIIPL Tdap with a margin of 10% compared to Boostrix® in terms of seroprotection rates against diphtheria 30 days after vaccination, in healthy subjects were demonstrated.
A seroprotected subject is defined as a subject with anti-DT antibody concentrations ≥ 0.1 IU/mL.
Seroprotection rates are calculated based on the number of subjects with a baseline and Day 30 result available, respectively.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

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

End point timeframe:

Day 0, Day 30

| **End point values** | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | | | | |
| Day 0 | 67.1 (63.87 to 70.16) | 67.7 (63.11 to 71.92) | | |
| Day 30 | 94.4 (92.63 to 95.73) | 94.9 (92.38 to 96.60) | | |

## Statistical analyses

| **Statistical analysis title** | SIIPL Tdap vs Boostrix® |
|---|---|

Statistical analysis description:

Difference between percentages of Seroprotection rates of SIIPL Tdap and Boostrix®(SIIPL Tdap - Boostrix®). 95% CI of seroprotection rate, booster response rate and difference (Diff.) are based on Wilson Score method.

| | |
|---|---|
| Comparison groups | SIIPL Tdap v Boostrix® |

| | |
|---|---|
| Number of subjects included in analysis | 1284 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Wilson Score method |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.96 |
| upper limit | 2.35 |

## Primary: Seroprotection rate against Tetanus toxoid (TT)

| | |
|---|---|
| End point title | Seroprotection rate against Tetanus toxoid (TT) |

End point description:

The non-inferiority of SIIPL Tdap with a margin of 10% compared to Boostrix® in terms of seroprotection rates against tetanus 30 days after vaccination, in healthy subjects were demonstrated. A seroprotected subject is defined as a subject with anti-TT antibody concentrations ≥ 0.1 IU/mL. Seroprotection rates are calculated based on the number of subjects with a baseline and Day 30 result available, respectively.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

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

End point timeframe:

Day 0, Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | | | | |
| Day 0 | 93.4 (91.58 to 94.92) | 95.1 (92.65 to 96.78) | | |
| Day 30 | 99.9 (99.34 to 99.98) | 100.0 (99.11 to 100.00) | | |

## Statistical analyses

| Statistical analysis title | SIIPL Tdap vs Boostrix® |
|---|---|

Statistical analysis description:

Difference between percentages of Seroprotection rates of SIIPL Tdap and Boostrix® (SIIPL Tdap - Boostrix®). 95% CI of seroprotection rate, booster response rate and difference (Diff.) are based on Wilson Score method.

| | |
|---|---|
| Comparison groups | SIIPL Tdap v Boostrix® |

| | |
|---|---|
| Number of subjects included in analysis | 1284 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Wilson Score method |
| Point estimate | -0.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.66 |
| upper limit | 0.77 |

## Primary: Booster response rate to Pertussis toxoid (PT)

| | |
|---|---|
| End point title | Booster response rate to Pertussis toxoid (PT) |

End point description:

The non-inferiority of SIIPL Tdap with a margin of 10% compared to Boostrix® in terms of booster response to pertussis toxoid (PT) 30 days after vaccination, in healthy subjects were demonstrated. Booster response rate is calculated based on the number of subjects with both baseline and Day 30 sample.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

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

End point timeframe:

Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 93.8 (91.97 to 95.22) | 88.4 (85.00 to 91.07) | | |

## Statistical analyses

| Statistical analysis title | SIIPL Tdap vs Boostrix® |
|---|---|

Statistical analysis description:

Difference between percentages of booster response rates of SIIPL Tdap and Boostrix® (SIIPL Tdap - Boostrix®). 95% CI of seropositive rates, booster response rates and difference (Diff.) are based on Wilson Score method.

| | |
|---|---|
| Comparison groups | Boostrix® v SIIPL Tdap |

| | |
|---|---|
| Number of subjects included in analysis | 1284 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Wilson Score method |
| Point estimate | 5.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.17 |
| upper limit | 9.09 |

## Primary: Booster response rate to Filamentous hemagglutinin (FHA)

| | |
|---|---|
| End point title | Booster response rate to Filamentous hemagglutinin (FHA) |

End point description:

The non-inferiority of SIIPL Tdap with a margin of 10% compared to Boostrix® in terms of booster response to filamentous hemagglutinin (FHA) 30 days after vaccination, in healthy subjects were demonstrated.
Booster response rate is calculated based on the number of subjects with both baseline and Day 30 sample.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

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

End point timeframe:

Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 89.7 (87.48 to 91.56) | 90.9 (87.84 to 93.29) | | |

## Statistical analyses

| Statistical analysis title | SIIPL Tdap vs Boostrix® |
|---|---|

Statistical analysis description:

Difference between percentages of booster response rates of SIIPL Tdap and Boostrix®(SIIPL Tdap - Boostrix®). 95% CI of seropositive rates, booster response rates and difference (Diff.) are based on Wilson Score method.

| | |
|---|---|
| Comparison groups | SIIPL Tdap v Boostrix® |

| | |
|---|---|
| Number of subjects included in analysis | 1284 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Wilson Score method |
| Point estimate | -1.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.48 |
| upper limit | 2.37 |

## Primary: Booster response rate to Pertactin (PRN)

| | |
|---|---|
| End point title | Booster response rate to Pertactin (PRN) |

End point description:

The non-inferiority of SIIPL Tdap with a margin of 10% compared to Boostrix® in terms of booster response to Pertactin (PRN) 30 days after vaccination, in healthy subjects were demonstrated. Booster response rate is calculated based on the number of subjects with both baseline and Day 30 sample. The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

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

End point timeframe:

Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 86.3 (83.83 to 88.44) | 84.4 (80.69 to 87.54) | | |

### Statistical analyses

| Statistical analysis title | SIIPL Tdap vs Boostrix® |
|---|---|

Statistical analysis description:

Difference between percentages of booster response rates of SIIPL Tdap and Boostrix® (SIIPL Tdap - Boostrix®). 95% CI of seropositive rates, booster response rates and difference (Diff.) are based on Wilson Score method.

| | |
|---|---|
| Comparison groups | SIIPL Tdap v Boostrix® |
| Number of subjects included in analysis | 1284 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Wilson Score method |
| Point estimate | 1.88 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.1 |
| upper limit | 6.18 |

## Secondary: Booster response rate to DT

| End point title | Booster response rate to DT |
|---|---|

End point description:

The booster response rates to SIIPL Tdap and Boostrix® vaccines, with respect to anti-DT, 30 days after vaccination, in healthy subjects were assesed. Booster response rate is calculated based on the number of subjects with both baseline and Day 30 sample.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 72.1 (69.03 to 75.03) | 78.6 (74.48 to 82.22) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Booster response rate to TT

| End point title | Booster response rate to TT |
|---|---|

End point description:

The booster response rates to SIIPL Tdap and Boostrix® vaccines, with respect to anti-TT, 30 days after vaccination, in healthy subjects were assessed. Booster response rate is calculated based on the number of subjects with both baseline and Day 30 sample.
All subjects who received study vaccine as per the assigned treatment group and had 30 days of postvaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 85.2 (82.71 to 87.47) | 87.0 (83.47 to 89.83) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric mean concentrations for anti-DT

| End point title | Geometric mean concentrations for anti-DT |
|---|---|

End point description:

The immune responses of SIIPL Tdap as compared to Boostrix® with respect to antibody GMC for anti-DT 30 days after vaccination, in healthy subjects were assesed.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 0, Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 0 | 0.16 (0.15 to 0.18) | 0.15 (0.13 to 0.18) | | |
| Day 30 | 1.03 (0.94 to 1.13) | 1.44 (1.26 to 1.65) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric mean concentrations for anti-TT

| End point title | Geometric mean concentrations for anti-TT |
|---|---|

End point description:

The immune responses of SIIPL Tdap as compared to Boostrix® with respect to antibody GMC for anti-TT 30 days after vaccination, in healthy subjects were assesed.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 0, Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 0 | 1.09 (0.98 to 1.21) | 1.16 (1.01 to 1.34) | | |
| Day 30 | 8.57 (8.13 to 9.04) | 8.87 (8.32 to 9.46) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric mean concentrations for anti-FHA

| End point title | Geometric mean concentrations for anti-FHA |
|---|---|

End point description:

The immune responses of SIIPL Tdap as compared to Boostrix® with respect to antibody GMC for anti-FHA 30 days after vaccination, in healthy subjects were assesed.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 0, Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 0 | 33.78 (31.16 to 36.62) | 35.03 (31.31 to 39.20) | | |
| Day 30 | 254.23 (241.33 to 267.81) | 361.45 (335.10 to 389.87) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric mean concentrations for anti-PRN

| End point title | Geometric mean concentrations for anti-PRN |
|---|---|

End point description:

The immune responses of SIIPL Tdap as compared to Boostrix® with respect to antibody GMC for anti-PRN 30 days after vaccination, in healthy subjects were assesed.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 0, Day 30

| **End point values** | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 0 | 32.52 (28.35 to 37.29) | 36.50 (29.80 to 44.70) | | |
| Day 30 | 618.32 (562.63 to 679.52) | 516.12 (456.10 to 584.05) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric mean concentrations for anti-PT

| End point title | Geometric mean concentrations for anti-PT |
|---|---|

End point description:

The immune responses of SIIPL Tdap as compared to Boostrix® with respect to antibody GMC for anti-PT 30 days after vaccination, in healthy subjects were assed.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 0, Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Day 0 | 8.78 (7.91 to 9.74) | 8.97 (7.82 to 10.29) | | |
| Day 30 | 112.77 (105.58 to 120.44) | 71.53 (65.09 to 78.61) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Seropositive subjects against pertussis antigens PT

| End point title | Seropositive subjects against pertussis antigens PT |
|---|---|

End point description:

The percentage of seropositive subjects against pertussis antigens (PT), i.e. with antibody titers ≥ LLOQ against each antigen 30 days after vaccination with SIIPL Tdap or Boostrix®, in healthy subjects were determined.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 0, Day 30

| End point values | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | | | | |
| Day 0 | 97.0 (95.58 to 97.91) | 97.9 (96.07 to 98.90) | | |
| Day 30 | 100.0 (99.55 to 100.00) | 100.0 (99.11 to 100.00) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Seropositive subjects against pertussis antigens FHA

| End point title | Seropositive subjects against pertussis antigens FHA |
|---|---|

End point description:

The percentage of seropositive subjects against pertussis antigens (FHA), i.e. with antibody titers ≥ LLOQ against each antigen 30 days after vaccination with SIIPL Tdap or Boostrix®, in healthy subjects were determined.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 0, Day 30

| **End point values** | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | | | | |
| Day 0 | 99.4 (98.64 to 99.75) | 99.8 (98.69 to 99.96) | | |
| Day 30 | 100.0 (99.55 to 100.0) | 100.0 (99.11 to 100.0) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Seropositive subjects against pertussis antigens PRN

| End point title | Seropositive subjects against pertussis antigens PRN |
|---|---|

End point description:

The percentage of seropositive subjects against pertussis antigens (PRN), i.e. with antibody titers ≥ LLOQ against each antigen 30 days after vaccination with SIIPL Tdap or Boostrix®, in healthy subjects were determined.
The per protocol set (PPS) consisted of all subjects who received study vaccine as per the assigned treatment group and had 30 days post-vaccination immunogenicity data with no major protocol deviations that were determined to potentially interfere with immune response to the study vaccine.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 0, Day 30

| **End point values** | SIIPL Tdap | Boostrix® | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854 | 430 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | | | | |
| Day 0 | 94.1 (92.36 to 95.53) | 93.7 (91.02 to 95.65) | | |
| Day 30 | 99.6 (98.97 to 99.88) | 99.8 (98.69 to 99.96) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Day 0 to Day 30 | |
| Assessment type | Non-systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |
| **Reporting groups** | |
| Reporting group title | SIIPL Tdap |
| Reporting group description: | |
| Subjects received SIIPL Tdap vaccine in phase II and Phase III period. | |
| Reporting group title | Boostrix® |
| Reporting group description: | |
| Subjects received Boostrix® vaccine in phase II and Phase III period. | |

| Serious adverse events | SIIPL Tdap | Boostrix® | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 887 (0.34%) | 1 / 445 (0.22%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Foetal death | | | |
| subjects affected / exposed | 0 / 887 (0.00%) | 1 / 445 (0.22%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Retinal detachment | | | |
| subjects affected / exposed | 1 / 887 (0.11%) | 0 / 445 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 1 / 887 (0.11%) | 0 / 445 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Appendicitis | | | |
| subjects affected / exposed | 1 / 887 (0.11%) | 0 / 445 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 3 %

| **Non-serious adverse events** | SIIPL Tdap | Boostrix® | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 667 / 887 (75.20%) | 339 / 445 (76.18%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 267 / 887 (30.10%) | 145 / 445 (32.58%) | |
| occurrences (all) | 291 | 169 | |
| Dizziness | | | |
| subjects affected / exposed | 97 / 887 (10.94%) | 41 / 445 (9.21%) | |
| occurrences (all) | 98 | 41 | |
| General disorders and administration site conditions | | | |
| Injection site pain | | | |
| subjects affected / exposed | 569 / 887 (64.15%) | 283 / 445 (63.60%) | |
| occurrences (all) | 578 | 286 | |
| Fatigue | | | |
| subjects affected / exposed | 319 / 887 (35.96%) | 140 / 445 (31.46%) | |
| occurrences (all) | 327 | 141 | |
| Malaise | | | |
| subjects affected / exposed | 134 / 887 (15.11%) | 62 / 445 (13.93%) | |
| occurrences (all) | 136 | 62 | |
| Injection site swelling | | | |
| subjects affected / exposed | 129 / 887 (14.54%) | 49 / 445 (11.01%) | |
| occurrences (all) | 129 | 49 | |
| Injection site erythema | | | |
| subjects affected / exposed | 100 / 887 (11.27%) | 41 / 445 (9.21%) | |
| occurrences (all) | 100 | 41 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 54 / 887 (6.09%)<br>56 | 34 / 445 (7.64%)<br>34 | |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 29 / 887 (3.27%)<br>29 | 14 / 445 (3.15%)<br>14 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 01 October 2019 | The amendment was written in response to the requests by the PEI to the clinical trial application according to the second sentence of Article 9(2) of the German GCP-Verordnung.<br>• Added details to indicate that the Phase II part of the ongoing Indian Phase II/III study had been completed. Independent DSMB reviewed safety data of 150 subjects and issued certificate to proceed with recruitment in the Phase III part of that study.<br>• Added an Emergency Unblinding section to describe unblinding to be performed by the investigator in emergency situations during the study to handle AEs, suspected unexpected serious adverse reaction or any other subject's safety concern, which the investigator deems necessary to break the blind. The new section also described the procedure for unblinding or breaking of randomization codes.<br>• Added a Study Termination Criteria Due to SAEs section to provide definition of study termination rules and the role of the DSMB in decision making in this process. |
| 06 December 2019 | The amendment was written in response to the requests by the Ethics Committee of the Medical Association of the State of Baden-Württemberg to the ethics application.<br>• Added two additional bullet points to inclusion criterion number 2 to define age limits of the study subject per phase of the study.<br>• Changed the inclusion criterion number 5, contraception, from "medically approved contraception" to "highly effective method of contraception". |
| 04 September 2020 | The amendment was mainly driven by the delayed availability of immunogenicity data for the analysis at the end of Phase II of the study for sample size determination for Phase III. The validation of the commercial assay kits originally selected for this study did not work as expected; therefore, the SIIPL initiated the validation of another suitable method.<br>•In March 2020, recruitment was put on hold due to the COVID-2019 pandemic after 378 subjects were randomized. As the recruitment of 411 adult subjects in the Phase II part of the study was not based on any statistical calculation, Phase II was considered<br>completed with 378 subjects randomized (of which 377 subjects received the study vaccine) instead of the 411 subjects stated in protocol Version 3.0, dated 06 December 2019.<br>•Removed the sample size re-calculation at the end of Phase II due to the delayed availability of immunogenicity data. Introduced the group sequential design to allow for conducting an interim analysis during Phase III when the immunogenicity data would be available.<br>• Due to the exceptional circumstances as a result of COVID-19, an additional follow-up phone call on Day 60 (+7 days) was added to determine the health status and to ask the subjects about potential SARS-CoV-2 infection during study participation.<br>• Added text to state that for Phase III, the Day 0 visit could be delayed, if required. A window of 10 days from the signing of the informed consent to enrolment on Day 0 was allowed.<br>• Added text to specify that blood pressure will not be measured in Cohorts 2 and 3.<br>• Added text to provide a brief summary of safety data of the Phase II part of the Phase II/III clinical study in India. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 27 March 2020 | As of 26 February 2020, the first adult subject was enrolled into the Phase II part of the study. On 11 March 2020, the World Health Organization (WHO) declared the novel coronavirus (COVID-19) outbreak a global pandemic.<br>On 23 Mar 2020, the Sponsor requested the DSMB to hold a meeting to discuss the impact of the COVID-19 pandemic on the study. On 25 Mar 2020, an ad-hoc Data Safety Monitoring Board (DSMB) meeting was held. As a consequence of the ongoing pandemic and as a precaution because the impact on the trial was unforeseeable at this timepoint, the DSMB recommended to temporarily hold on the recruitment of any new subjects. On 27 March 2020, the Sponsor notified the investigators of the hold on recruitment of new subjects. At that time, 377 subjects had received a study vaccine, which was considered sufficient to conclude the Phase II part of the study. These subjects were carefully monitored and safely followed up until the Day 30 visit as per the protocol and in accordance with the national RKI guidance.<br>On 11 Sep 2020, the DSMB recommended the study be continued based on its review of the safety data of the 377 subjects, finding no safety signals and a similar reactogenicity profile between the two vaccines. | 03 November 2020 |

Notes:

## Limitations and caveats

None reported