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 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 Units: years			
arithmetic mean	37.9	37.5	
standard deviation	± 15.83	± 16.0	-
Gender categorical 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 occurrences (all)	54 / 887 (6.09%) 56	34 / 445 (7.64%) 34	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	29 / 887 (3.27%) 29	14 / 445 (3.15%) 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. • 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. • 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. • 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. • Added two additional bullet points to inclusion criterion number 2 to define age limits of the study subject per phase of the study. • 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. •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 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. •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. • 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. • 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. • Added text to specify that blood pressure will not be measured in Cohorts 2 and 3. • 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. 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. 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