Clinical trial results:
Double-Blind, Randomized, Placebo-Controlled Phase III Clinical Trial to Evaluate Efficacy and Safety of a Dengue 1, 2, 3, 4 (Attenuated) Vaccine produced by Instituto Butantan

Summary

EudraCT number	2022-003868-25
Trial protocol	Outside EU/EEA
Global end of trial date	06 June 2025

Results information

Result version number	v1 (current)
This version publication date	24 December 2025
First version publication date	24 December 2025

Trial information

Trial identification

Sponsor protocol code	DEN-03-IB

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02406729
WHO universal trial number (UTN)	-
Other trial identifiers	UTN: U1111-1168-8679

Notes:

Sponsors

Sponsor organisation name	Butantan Institute
Sponsor organisation address	Av. Vital Brasil, 1500, Butantã, São Paulo, Brazil, 05503-900
Public contact	Butantan Institute, Butantan Institute, 11 3723 2121,
Scientific contact	Butantan Institute, Butantan Institute, 11 3723 2121,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002999-PIP01-21
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	14 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 July 2021
Global end of trial reached?	Yes
Global end of trial date	06 June 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The goal of this study is to learn how well the Dengue 1,2,3,4 (attenuated) vaccine works at helping the body make antibodies against the 4 types of dengue virus (DENV) in participants aged 2 to 59 years old. Researchers also want to learn about the safety of V181 and how well older adults tolerate it.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 February 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 16235
Worldwide total number of subjects	16235
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)	7812
Adolescents (12-17 years)	2351
Adults (18-64 years)	6072
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Healthy participants between 2 and 59 years of age were enrolled into this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dengue 1,2,3,4 (Attenuated) Vaccine

Arm description:

Participants received a single 0.5 mL subcutaneous (SC) dose of dengue 1,2,3,4 (attenuated) vaccine.

Arm type	Experimental
Investigational medicinal product name	Dengue 1,2,3,4 (Attenuated) Vaccine
Investigational medicinal product code	
Other name	Butantan DV TetraVax-DV-TV003
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL dose containing 1000 plaque-forming units per vaccine virus (1,2,3,4).

Arm title	Placebo

Arm description:

Participants received a single 0.5 mL SC dose of placebo.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL dose of dengue 1,2,3,4 (attenuated) vaccine-matching placebo.

Number of subjects in period 1	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo
Started	10259	5976
Completed	8801	5092
Not completed	1458	884
Physician decision	11	6

Consent withdrawn by subject	753	450
Not Reported	28	13
Death	43	34
Lost to follow-up	617	380
Consent withdrawn by Parent/Guardian	6	1

Baseline characteristics

Reporting groups	
Reporting group title	Dengue 1,2,3,4 (Attenuated) Vaccine
Reporting group description:	
Participants received a single 0.5 mL subcutaneous (SC) dose of dengue 1,2,3,4 (attenuated) vaccine.	
Reporting group title	Placebo
Reporting group description:	
Participants received a single 0.5 mL SC dose of placebo.	

Reporting group values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo	Total
Number of subjects	10259	5976	16235
Age Categorical Units: Participants			
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)	5185	2627	7812
Adolescents (12-17 years)	1528	823	2351
Adults (18-64 years)	3546	2526	6072
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	18.4	20.7	
standard deviation	± 16.6	± 17.1	-
Gender Categorical Units: Participants			
Female	5554	3213	8767
Male	4705	2763	7468
Age Group			
Randomization of participants was stratified by age groups of 2 to 6 years of age, 7 to 17 years of age, or 18 to 59 years of age.			
Units: Subjects			
2 to 6 years of age	3337	1679	5016
7 to 17 years of age	3376	1771	5147
18 to 59 years of age	3546	2526	6072

End points

End points reporting groups

Reporting group title	Dengue 1,2,3,4 (Attenuated) Vaccine
Reporting group description:	
Participants received a single 0.5 mL subcutaneous (SC) dose of dengue 1,2,3,4 (attenuated) vaccine.	
Reporting group title	Placebo
Reporting group description:	
Participants received a single 0.5 mL SC dose of placebo.	

Primary: Incidence Rate of Virologically Confirmed Dengue (VCD) Cases Regardless of Prior Exposure to Dengue Virus

End point title	Incidence Rate of Virologically Confirmed Dengue (VCD) Cases Regardless of Prior Exposure to Dengue Virus
End point description:	
The incidence rate of VCD cases was defined as the number of VCD cases per 100 person-years at risk. The person-years at risk of each individual participant is the cumulative time (in years) until the participant was diagnosed with first symptomatic VCD episode or until the end of the study for each participant, whichever came first. The incidence rate for any serotype of dengue virus was reported. The analysis population consisted of the randomized participants, regardless of their prior exposure to dengue virus, who met the inclusion criteria and did not meet any exclusion criteria, received the investigational product to which they were randomized in accordance with the handling and administration conditions recommended by the manufacturer, did not use restricted medications, as per the protocol, and did not withdraw informed consent.	
End point type	Primary
End point timeframe:	
Up to approximately 28 days postvaccination	

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10209	5940		
Units: Cases per 100 Person-Years at Risk				
number (confidence interval 95%)	0.376 (0.323 to 0.436)	1.074 (0.954 to 1.205)		

Statistical analyses

Statistical analysis title	Vaccine Efficacy Percentage
Statistical analysis description:	
Vaccine efficacy was estimated based on the exact binomial method proposed by Chan and Bohidar, the 95% confidence interval (CI) was estimated using Blaker's exact CI, and p-value were estimated from binomial exact method. The statistical criterion for success requires the lower bound of the 2-sided 95% CI for vaccine efficacy to be > 25%.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	16149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Binomial Exact Method
Parameter estimate	Vaccine Efficacy Percent
Point estimate	64.974
Confidence interval	
level	95 %
sides	2-sided
lower limit	57.797
upper limit	71.024

Primary: Number of Participants who Experienced a Solicited Adverse Drug Reaction (ADR) Through 21 Days Postvaccination

End point title	Number of Participants who Experienced a Solicited Adverse Drug Reaction (ADR) Through 21 Days Postvaccination

End point description:

An ADR was defined as an adverse event (AE) that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited administration site ADRs included erythema(redness), induration, pain, pruritus, and swelling. Solicited systemic ADRs included arthralgia, chills, eye pain (retro-orbital pain), fatigue (asthenia), headache, myalgia (muscle pain), nausea, photophobia, pruritus, pyrexia (fever), skin rash (exanthema), and vomiting. The number of participants who experienced a solicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Primary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10259	5976		
Units: Participants				
number (not applicable)				
Administration Site Erythema	326	94		
Administration Site Induration	201	96		
Administration Site Pain	1536	672		
Administration Site Pruritus	587	244		
Administration Site Swelling	131	68		
Arthralgia	1162	491		
Chills	884	335		
Eye Pain	1636	645		
Fatigue	1995	912		
Headache	3768	1860		
Myalgia	1816	766		

Nausea	1257	634		
Photophobia	1000	488		
Pruritus	1977	532		
Pyrexia	1047	398		
Skin Rash	2326	253		
Vomiting	580	298		

Statistical analyses

Statistical analysis title	Dif in %-Administration Site Erythema

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.1

Statistical analysis title	Dif in %-Administration Site Induration

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.098
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.8

Statistical analysis title	Dif in %-Administration Site Pain

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	4.7

Statistical analysis title	Dif in %-Administration Site Pruritus

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference of Percentage
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2.3

Statistical analysis title	Dif in %-Administration Site Swelling

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from

the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.356
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.5

Statistical analysis title	Dif in %-Arthralgia

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	4.9

Statistical analysis title	Dif in %-Chills

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	4.3

Statistical analysis title	Dif in %-Eye Pain

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.9
upper limit	7

Statistical analysis title	Dif in %-Fatigue

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	5.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.1
upper limit	6.4

Statistical analysis title	Dif in %-Nausea

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	3.1

Statistical analysis title	Dif in %-Myalgia

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	7.1

Statistical analysis title	Dif in %-Headache

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.5
upper limit	8.4

Statistical analysis title	Dif in %-Photophobia

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	3

Statistical analysis title	Dif in %-Pyrexia

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	4.1

Statistical analysis title	Dif in %-Pruritus

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	10.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.9
upper limit	11.9

Statistical analysis title	Dif in %-Skin Rash

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	18.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	17.7
upper limit	19.6

Statistical analysis title	Dif in %-Vomiting

Statistical analysis description:

Estimated differences, CIs, and p-value are calculated based on Miettinen & Nurminen method stratified by age group (2 to 6 years, 7 to 17 years or 18 to 59 years); if no participants are in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum is excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.182
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	1.2

Primary: Number of Participants who Experienced an Unsolicited ADR Through 21 Days Postvaccination

End point title	Number of Participants who Experienced an Unsolicited ADR Through 21 Days Postvaccination

End point description:

An ADR was defined as an adverse event (AE) that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants who experienced an unsolicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Primary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10259	5976		
Units: Participants				
number (not applicable)	1386	719		

Statistical analyses

Statistical analysis title	Difference in %-Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method stratified by age group; if no participants were in one of the vaccination groups involved in a comparison for a particular stratum, then that stratum was excluded from the vaccination comparison.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	3

Secondary: Incidence Rate of VCD Cases in Participants with Prior Exposure to Dengue Fever

End point title	Incidence Rate of VCD Cases in Participants with Prior Exposure to Dengue Fever

End point description:

The incidence rate of VCD cases was defined as the number of VCD cases per 100 person-years at risk. The person-years at risk of each individual participant is the cumulative time (in years) until the participant was diagnosed with first symptomatic VCD episode or until the end of the study for each participant, whichever came first. The incidence rate for any serotype of dengue virus was reported. The analysis population consisted of the randomized participants with prior exposure to dengue virus who met the inclusion criteria and did not meet any exclusion criteria, received the investigational product to which they were randomized in accordance with the handling and administration conditions recommended by the manufacturer, did not use restricted medications, as per the protocol, and did not withdraw informed consent.

End point type	Secondary

End point timeframe:

Up to approximately 28 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4985	3023		
Units: Percentage of Participants				
number (confidence interval 95%)	0.198 (0.145 to 0.264)	0.863 (0.715 to 1.032)		

Statistical analyses

Statistical analysis title	Vaccine Efficacy %

Statistical analysis description:

Vaccine efficacy was estimated based on the exact binomial method proposed by Chan and Bohidar, the 95% CI was estimated using Blaker's exact CI, and p-values were estimated from binomial exact method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8008
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Binomial Exact Method
Parameter estimate	Vaccine Efficacy Percent
Point estimate	77.058
Confidence interval	
level	95 %
sides	2-sided
lower limit	67.552
upper limit	83.867

Secondary: Incidence Rate of VCD Cases in Participants without Prior Exposure to Dengue Fever

End point title	Incidence Rate of VCD Cases in Participants without Prior Exposure to Dengue Fever

End point description:

The incidence rate of VCD cases was defined as the number of VCD cases per 100 person-years at risk. The person-years at risk of each individual participant is the cumulative time (in years) until the participant was diagnosed with first symptomatic VCD episode or until the end of the study for each participant, whichever came first. The incidence rate for any serotype of dengue virus was reported. The analysis population consisted of the randomized participants without prior exposure to dengue virus who met the inclusion criteria and did not meet any exclusion criteria, received the investigational product to which they were randomized in accordance with the handling and administration conditions recommended by the manufacturer, did not use restricted medications, as per the protocol, and did not withdraw informed consent.

End point type	Secondary

End point timeframe:

Up to approximately 28 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4819	2678		
Units: Percentage of Participants				
number (confidence interval 95%)	0.571 (0.475 to 0.680)	1.387 (1.185 to 1.614)		

Statistical analyses

Statistical analysis title	Vaccine Efficacy Percentage

Statistical analysis description:

Vaccine efficacy was estimated based on the exact binomial method proposed by Chan and Bohidar, the 95% CI was estimated using Blaker's exact CI, and p-value were estimated from binomial exact method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7497
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0019
Method	Binomial Exact Method
Parameter estimate	Vaccine Efficacy Percent
Point estimate	58.855
Confidence interval	
level	95 %
sides	2-sided
lower limit	47.971
upper limit	67.554

Secondary: Incidence Rate of VCD Cases Reported by Viral Serotype

End point title	Incidence Rate of VCD Cases Reported by Viral Serotype

End point description:

The incidence rate of VCD cases was defined as the number of VCD cases per 100 person-years at risk. The person-years at risk of each individual participant is the cumulative time (in years) until the participant was diagnosed with first symptomatic VCD episode or until the end of the study for each participant, whichever came first. The incidence rate for each serotype of dengue virus was reported. Only dengue virus serotypes 1 and 2 were detected in this study. The analysis population consisted of the randomized participants who met the inclusion criteria and did not meet any exclusion criteria, received the investigational product to which they were randomized in accordance with the handling and administration conditions recommended by the manufacturer, did not use restricted medications, as per the protocol, and did not withdraw informed consent.

End point type	Secondary

End point timeframe:

Up to approximately 28 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10209	5940		
Units: Cases per 100 Person-Years at Risk				
number (confidence interval 95%)				
Dengue Virus Serotype 1	0.159 (0.125 to 0.199)	0.588 (0.500 to 0.686)		
Dengue Virus Serotype 2	0.216 (0.176 to 0.263)	0.489 (0.409 to 0.579)		

Statistical analyses

Statistical analysis title	Vaccine Efficiency %-DENV2

Statistical analysis description:

Vaccine efficacy was estimated based on the exact binomial method proposed by Chan and Bohidar, the 95% CI was estimated using Blaker's exact CI, and p-value were estimated from binomial exact method. The statistical criterion for success requires the lower bound of the 2-sided 95% CI for vaccine efficacy to be > 25%.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Binomial Exact Method
Parameter estimate	Vaccine Efficiency %
Point estimate	55.733
Confidence interval	
level	95 %
sides	2-sided
lower limit	42.339
upper limit	66.122

Statistical analysis title	Vaccine Efficacy %-DENV1

Statistical analysis description:

Vaccine efficacy was estimated based on the exact binomial method proposed by Chan and Bohidar, the 95% CI was estimated using Blaker's exact CI, and p-value were estimated from binomial exact method. The statistical criterion for success requires the lower bound of the 2-sided 95% CI for vaccine efficacy to be > 25%.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Binomial Exact Method
Parameter estimate	Vaccine Efficiency %
Point estimate	72.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	64.329
upper limit	79.664

Secondary: Incidence Rate of VCD Cases with Severe Dengue and/or Dengue with Warning Signs

End point title	Incidence Rate of VCD Cases with Severe Dengue and/or Dengue with Warning Signs

End point description:

The incidence rate of VCD cases was defined as the number of VCD cases per 100 person-years at risk. The person-years at risk of each individual participant is the cumulative time (in years) until the participant was diagnosed with first symptomatic VCD episode or until the end of the study for each participant, whichever came first. The incidence rate for any serotype of dengue virus was reported. The analysis population consisted of the randomized participants with warning signs or severe dengue who met the inclusion criteria and did not meet any exclusion criteria, received the investigational product to which they were randomized in accordance with the handling and administration conditions recommended by the manufacturer, did not use restricted medications, as per the protocol, and did not withdraw informed consent.

End point type	Secondary

End point timeframe:

Up to approximately 28 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10209	5940		
Units: Cases per 100 Person/Years				
number (confidence interval 95%)	0.013 (0.005 to 0.028)	0.065 (0.039 to 0.103)		

Statistical analyses

Statistical analysis title	Vaccine Efficacy Percentage

Statistical analysis description:

Vaccine efficacy was estimated based on the exact binomial method proposed by Chan and Bohidar, the 95% CI was estimated using Blaker’s exact CI, and p-value were estimated from binomial exact method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	16149
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0019
Method	Binomial Exact Method
Parameter estimate	Vaccine Efficacy Percentage
Point estimate	80.511

Confidence interval	
level	95 %
sides	2-sided
lower limit	50.828
upper limit	92.409

Secondary: Number of Participants Between 2 and 6 Years of Age who Experienced a Solicited ADR

End point title	Number of Participants Between 2 and 6 Years of Age who Experienced a Solicited ADR

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited administration site ADRs included erythema(redness), induration, pain, pruritus, and swelling. Solicited systemic ADRs included arthralgia, chills, eye pain (retro-orbital pain), fatigue (asthenia), headache, myalgia (muscle pain), nausea, photophobia, pruritus, pyrexia (fever), skin rash (exanthema), and vomiting. The number of participants between 2 and 6 years of age who experienced a solicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants from 2 to 6 years of age who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3337	1679		
Units: Participants				
Administration Site Erythema	53	29		
Administration Site Induration	55	39		
Administration Site Pain	365	181		
Administration Site Pruritus	95	51		
Administration Site Swelling	30	17		
Arthralgia	92	39		
Chills	111	46		
Eye Pain	119	43		
Fatigue	255	105		
Headache	622	259		
Myalgia	148	51		
Nausea	192	80		
Photophobia	76	38		
Pruritus	438	85		
Pyrexia	384	161		
Skin Rash	647	66		
Vomiting	241	114		

Statistical analyses

Statistical analysis title	Dif in %-Administration Site Erythema
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.714
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.6

Statistical analysis title	Dif in %-Administration Site Induration
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.096
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.1

Statistical analysis title	Dif in %-Administration Site Pain
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.866
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.9

Statistical analysis title	Dif in %-Administration Site Pruritus
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.705
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.8

Statistical analysis title	Dif in %-Administration Site Swelling
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.694
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.4

Statistical analysis title	Dif in %-Arthralgia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.363
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.3

Statistical analysis title	Dif in %-Chills
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.26
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.5

Statistical analysis title	Dif in %-Eye Pain
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.057
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2

Statistical analysis title	Dif in %-Fatigue
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.072
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	2.8

Statistical analysis title	Dif in %-Photophobia
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.975
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.8

Statistical analysis title	Dif in %-Nausea
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.144
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	2.2

Statistical analysis title	Dif in %-Myalgia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.017
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	2.4

Statistical analysis title	Dif in %-Headache
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	5.4

Statistical analysis title	Dif in %-Pyrexia
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.039
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	3.7

Statistical analysis title	Dif in %-Pruritus
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.5
upper limit	9.6

Statistical analysis title	Dif in %-Skin Rash
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	15.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.8
upper limit	17.1

Statistical analysis title	Dif in %-Vomiting
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.573
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.9

Secondary: Number of Participants Between 2 and 6 Years of Age who Experienced an Unsolicited ADR

End point title	Number of Participants Between 2 and 6 Years of Age who Experienced an Unsolicited ADR

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants between 2 and 6 years of age who experienced an unsolicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants between 2 and 6 years of age who received at least 1 dose of study intervention according to the study intervention they

received.

End point type	Secondary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3337	1679		
Units: Participants	316	148		

Statistical analyses

Statistical analysis title	Difference in %-Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.45
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.3

Secondary: Number of Participants Between 7 and 17 Years of Age who Experienced a Solicited ADR

End point title	Number of Participants Between 7 and 17 Years of Age who Experienced a Solicited ADR

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited administration site ADRs included erythema(redness), induration, pain, pruritus, and swelling. Solicited systemic ADRs included arthralgia, chills, eye pain (retro-orbital pain), fatigue (asthenia), headache, myalgia (muscle pain), nausea, photophobia, pruritus, pyrexia (fever), skin rash (exanthema), and vomiting. The number of participants between 7 and 17 years of age who experienced a solicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants between 7 and 17 years of age who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:
Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3376	1771		
Units: Participants				
Administration Site Erythema	93	33		
Administration Site Induration	50	22		
Administration Site Pain	641	251		
Administration Site Pruritus	254	107		
Administration Site Swelling	44	19		
Arthralgia	302	111		
Chills	252	89		
Eye Pain	654	225		
Fatigue	654	273		
Headache	1402	612		
Myalgia	555	239		
Nausea	460	230		
Photophobia	389	173		
Pruritus	646	148		
Pyrexia	362	131		
Skin Rash	746	66		
Vomiting	199	84		

Statistical analyses

Statistical analysis title	Dif in %-Administration Site Erythema
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.049
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1.7

Statistical analysis title	Dif in %-Administration Site Induration
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.488
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.9

Statistical analysis title	Dif in %-Administration Site Pain
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	6.9

Statistical analysis title	Dif in %-Administration Site Pruritus
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.048
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2.9

Statistical analysis title	Dif in %-Administration Site Swelling
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.475
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.8

Statistical analysis title	Dif in %-Arthralgia
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	4.1

Statistical analysis title	Dif in %-Eye Pain
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.6
upper limit	8.7

Statistical analysis title	Dif in %-Chills
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	3.8

Statistical analysis title	Dif in %-Fatigue
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	6.1

Statistical analysis title	Dif in %-Myalgia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	4.9

Statistical analysis title	Dif in %-Headache
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.2
upper limit	9.7

Statistical analysis title	Dif in %-Nausea
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.523
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	2.6

Statistical analysis title	Dif in %-Photophobia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.055
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3.5

Statistical analysis title	Dif in %-Pruritus
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	10.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.9
upper limit	12.6

Statistical analysis title	Dif in %-Skin Rash
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	18.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.7
upper limit	20

Statistical analysis title	Dif in %-Pyrexia
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	4.9

Statistical analysis title	Dif in %-Vomiting
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.085
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	2.4

Secondary: Number of Participants Between 7 and 17 Years of Age who Experienced an Unsolicited ADR

End point title	Number of Participants Between 7 and 17 Years of Age who Experienced an Unsolicited ADR
End point description:	
An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants between 7 and 17 years of age who experienced an unsolicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants between 7 and 17 years of age who received at least 1 dose of study intervention according to the study intervention they received.	
End point type	Secondary
End point timeframe:	
Up to approximately 21 days postvaccination	

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3376	1771		
Units: Participants	371	193		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.92
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.8

Secondary: Number of Participants Between 18 and 59 Years of Age who Experienced a Solicited ADR

End point title	Number of Participants Between 18 and 59 Years of Age who Experienced a Solicited ADR

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited administration site ADRs included erythema(redness), induration, pain, pruritus, and swelling. Solicited systemic ADRs included arthralgia, chills, eye pain (retro-orbital pain), fatigue (asthenia), headache, myalgia (muscle pain), nausea, photophobia, pruritus, pyrexia (fever), skin rash (exanthema), and vomiting. The number of participants between 18 and 59 years of age who experienced a solicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants between 18 and 59 years of age who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3546	2526		
Units: Participants				
Administration Site Erythema	180	32		
Administration Site Induration	96	35		
Administration Site Pain	530	240		
Administration Site Pruritus	238	86		
Administration Site Swelling	57	32		
Arthralgia	768	341		
Chills	521	200		

Eye Pain	863	377		
Fatigue	1086	534		
Headache	1744	989		
Myalgia	1113	476		
Nausea	605	324		
Photophobia	535	277		
Pruritus	893	299		
Pyrexia	301	106		
Skin Rash	933	121		
Vomiting	140	100		

Statistical analyses

Statistical analysis title	Dif in %-Administration Site Erythema
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	4.7

Statistical analysis title	Dif in %-Administration Site Induration
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2

Statistical analysis title	Dif in %-Administration Site Pain
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	7.1

Statistical analysis title	Dif in %-Administration Site Pruritus
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	4.4

Statistical analysis title	Dif in %-Administration Site Swelling
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.276
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.9

Statistical analysis title	Dif in %-Arthralgia
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	8.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.2
upper limit	10

Statistical analysis title	Dif in %-Chills
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.2
upper limit	8.3

Statistical analysis title	Dif in %-Eye Pain
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.4
upper limit	11.4

Statistical analysis title	Dif in %-Fatigue
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	9.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.3
upper limit	11.7

Statistical analysis title	Dif in %-Nausea
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	6

Statistical analysis title	Dif in %-Myalgia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.4
upper limit	14.7

Statistical analysis title	Dif in %-Headache
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.5
upper limit	12.5

Statistical analysis title	Dif in %-Photophobia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	5.8

Statistical analysis title	Dif in %-Skin Rash
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	21.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.9
upper limit	23.2

Statistical analysis title	Dif in %-Pyrexia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	5.5

Statistical analysis title	Dif in %-Pruritus
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	13.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.4
upper limit	15.2

Statistical analysis title	Dif in %-Vomiting
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.983
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1

Secondary: Number of Participants Between 18 and 59 Years of Age who Experienced an Unsolicited ADR

End point title	Number of Participants Between 18 and 59 Years of Age who Experienced an Unsolicited ADR

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants between 18 and 59 years of age who experienced an unsolicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants between 18 and 59 years of age who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3546	2526		
Units: Participants	699	378		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	6.6

Secondary: Number of Participants with Prior Exposure to Any Serotype of Dengue

Virus who Experienced a Solicited ADR

End point title	Number of Participants with Prior Exposure to Any Serotype of Dengue Virus who Experienced a Solicited ADR

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited administration site ADRs included erythema(redness), induration, pain, pruritus, and swelling. Solicited systemic ADRs included arthralgia, chills, eye pain (retro-orbital pain), fatigue (asthenia), headache, myalgia (muscle pain), nausea, photophobia, pruritus, pyrexia (fever), skin rash (exanthema), and vomiting. The number of participants with prior exposure to any serotype of dengue virus who experienced a solicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants with prior exposure to dengue virus who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5010	3046		
Units: Participants				
Administration Site Erythema	118	47		
Administration Site Induration	95	48		
Administration Site Pain	779	339		
Administration Site Pruritus	288	131		
Administration Site Swelling	67	33		
Arthralgia	608	299		
Chills	389	195		
Eye Pain	777	406		
Fatigue	986	530		
Headache	1957	1088		
Myalgia	913	474		
Nausea	645	379		
Photophobia	499	311		
Pruritus	858	296		
Pyrexia	372	188		
Skin Rash	850	125		
Vomiting	235	147		

Statistical analyses

Statistical analysis title	Dif in %-Administration Site Erythema

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.021
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	1.4

Statistical analysis title	Dif in %-Administration Site Induration
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.317
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.9

Statistical analysis title	Dif in %-Administration Site Pain
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	5.5

Statistical analysis title	Dif in %-Administration Site Pruritus
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.014
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	2.2

Statistical analysis title	Dif in %-Administration Site Swelling
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.25
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.8

Statistical analysis title	Dif in %-Arthralgia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	4.4

Statistical analysis title	Dif in %-Chills
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.8

Statistical analysis title	Dif in %-Eye Pain
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	4

Statistical analysis title	Dif in %-Fatigue
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	4.6

Statistical analysis title	Dif in %-Pruritus
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.2
upper limit	9.1

Statistical analysis title	Dif in %-Photophobia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.894
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.2

Statistical analysis title	Dif in %-Headache
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	6.2

Statistical analysis title	Dif in %-Myalgia
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	5.1

Statistical analysis title	Dif in %-Nausea
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.414
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	2.1

Statistical analysis title	Dif in %-Pyrexia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.103
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	2.1

Statistical analysis title	Dif in %-Skin Rash
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.5
upper limit	14.1

Statistical analysis title	Dif in %-Vomiting
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.54
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.7

Secondary: Number of Participants with Prior Exposure to Any Serotype of Dengue Virus who Experienced an Unsolicited ADR

End point title	Number of Participants with Prior Exposure to Any Serotype of Dengue Virus who Experienced an Unsolicited ADR

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants with prior exposure to any serotype of dengue virus who experienced an unsolicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants with prior exposure to any serotype of dengue virus who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5010	3046		
Units: Participants	667	401		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.434
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	2.1

Secondary: Number of Participants Without Prior Exposure to Any Serotype of Dengue Virus who Experienced a Solicited ADR

End point title	Number of Participants Without Prior Exposure to Any Serotype of Dengue Virus who Experienced a Solicited ADR

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited administration site ADRs included erythema(redness), induration, pain, pruritus, and swelling. Solicited systemic ADRs included arthralgia, chills, eye pain (retro-orbital pain), fatigue (asthenia), headache, myalgia (muscle pain), nausea, photophobia, pruritus, pyrexia (fever), skin rash (exanthema), and vomiting. The number of participants without prior exposure to any serotype of dengue virus who experienced a solicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants without prior exposure to dengue virus who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4843	2690		
Units: Participants				
Administration Site Erythema	201	42		
Administration Site Induration	99	42		
Administration Site Pain	687	304		
Administration Site Pruritus	274	106		
Administration Site Swelling	57	32		
Arthralgia	494	165		
Chills	450	124		
Eye Pain	782	207		
Fatigue	917	345		
Headache	1647	684		
Myalgia	815	263		
Nausea	562	232		
Photophobia	449	152		
Pruritus	1039	209		
Pyrexia	632	188		
Skin Rash	1387	115		
Vomiting	327	145		

Statistical analyses

Statistical analysis title	Dif in %-Administration Site Erythema
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	3.6

Statistical analysis title	Dif in %-Administration Site Induration
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.119
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	1.1

Statistical analysis title	Dif in %-Administration Site Pain
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	4.5

Statistical analysis title	Dif in %-Administration Site Pruritus
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	2.9

Statistical analysis title	Dif in %-Administration Site Swelling
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.999
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.5

Statistical analysis title	Dif in %-Arthralgia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	6.2

Statistical analysis title	Dif in %-Chills
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.1
upper limit	6.4

Statistical analysis title	Dif in %-Eye Pain
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	9.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	8
upper limit	10.9

Statistical analysis title	Dif in %-Fatigue
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.7
upper limit	8.9

Statistical analysis title	Dif in %-Pruritus
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	14.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.9
upper limit	16

Statistical analysis title	Dif in %-Photophobia
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	5.5

Statistical analysis title	Dif in %-Headache
Statistical analysis description: Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	10.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.1
upper limit	12

Statistical analysis title	Dif in %-Myalgia
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.9
upper limit	9.8

Statistical analysis title	Dif in %-Nausea
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.1
upper limit	4.9

Statistical analysis title	Dif in %-Pyrexia
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.5
upper limit	7.2

Statistical analysis title	Dif in %-Skin Rash
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo
Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	25
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.5
upper limit	26.5

Statistical analysis title	Dif in %-Vomiting
Statistical analysis description:	
Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.	
Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.035
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	2.3

Secondary: Number of Participants Without Prior Exposure to Any Serotype of Dengue Virus who Experienced an Unsolicited ADR

End point title	Number of Participants Without Prior Exposure to Any Serotype of Dengue Virus who Experienced an Unsolicited ADR

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants without prior exposure to any serotype of dengue virus who experienced an unsolicited ADR within the first 21 days postvaccination was reported. The population analyzed was all randomized participants without prior exposure to any serotype of dengue virus who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 21 days postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4843	2690		
Units: Participants	663	284		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.1
upper limit	5.1

Secondary: Number of Participants who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point title	Number of Participants who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants who experienced an unsolicited ADR from day 22 postvaccination through the duration of the study was reported. The population analyzed was all randomized participants without prior exposure to any serotype of dengue virus who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 5 years postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10259	5976		
Units: Participants	23	15		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	16235
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.996
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.1

Secondary: Number of Participants Between 2 and 6 Years of Age who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point title	Number of Participants Between 2 and 6 Years of Age who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants from 2 to 6 years of age who experienced an unsolicited ADR from day 22 postvaccination through the duration of the study was reported. The population analyzed was all randomized participants from 2 to 6 years of age without prior exposure to any serotype of dengue virus who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 5 years postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3337	1679		
Units: Participants	3	0		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	5016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.219
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.3

Secondary: Number of Participants Between 7 and 17 Years of Age who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point title	Number of Participants Between 7 and 17 Years of Age who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants from the ages of 7 to 17 years of age who experienced an unsolicited ADR from day 22 postvaccination through the duration of the study was reported. The population analyzed was all randomized participants between 7 and 17 without prior exposure to any serotype of dengue virus who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 5 years postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3376	1771		
Units: Participants	6	3		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	5147
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.946
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.2

Secondary: Number of Participants Between 18 and 59 Years of Age who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point title	Number of Participants Between 18 and 59 Years of Age who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants between 18 and 59 years of age who experienced an unsolicited ADR from day 22 postvaccination through the duration of the study was reported. The population analyzed was all randomized participants between 18 and 59 years of age who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 5 years postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3546	2526		
Units: Participants	14	12		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	6072
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.637
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.3

Secondary: Number of Participants With Prior Exposure to Any Serotype of Dengue Virus who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point title	Number of Participants With Prior Exposure to Any Serotype of Dengue Virus who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants with prior exposure to dengue virus who experienced an unsolicited ADR from day 22 postvaccination through the duration of the study was reported. The population analyzed was all randomized participants with prior exposure to dengue virus without prior exposure to any serotype of dengue virus who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 5 years postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5010	3046		
Units: Participants	9	5		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	8056
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.838
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.2

Secondary: Number of Participants Without Prior Exposure to Any Serotype of Dengue Virus who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point title	Number of Participants Without Prior Exposure to Any Serotype of Dengue Virus who Experienced an Unsolicited ADR from Day 22 Postvaccination through the Duration of the Study

End point description:

An ADR was defined as an AE that had a reasonable causal link with the vaccination. An AE was any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. The number of participants without prior exposure to any serotype of dengue virus who experienced an unsolicited ADR from day 22 postvaccination through the duration of the study was reported. The population analyzed was all randomized participants without prior exposure to any serotype of dengue virus, without prior exposure to any serotype of dengue virus who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary

End point timeframe:

Up to approximately 5 years postvaccination

End point values	Dengue 1,2,3,4 (Attenuated) Vaccine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4843	2690		
Units: Participants	11	9		

Statistical analyses

Statistical analysis title	Difference in Percentage - Unsolicited AEs

Statistical analysis description:

Estimated differences, CIs, and p-value were calculated based on Miettinen & Nurminen method.

Comparison groups	Dengue 1,2,3,4 (Attenuated) Vaccine v Placebo

Number of subjects included in analysis	7533
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.625
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	2

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 9 years

Adverse event reporting additional description:

All-cause Mortality: randomized participants; Adverse Events: randomized participants who received at least 1 dose of study intervention according to the study intervention they received

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received a single 0.5 mL SC dose of placebo.

Reporting group title	Dengue 1,2,3,4 (Attenuated) Vaccine

Reporting group description:

Participants received a single 0.5 mL subcutaneous (SC) dose of dengue 1,2,3,4 (attenuated) vaccine.

Serious adverse events	Placebo	Dengue 1,2,3,4 (Attenuated) Vaccine	
Total subjects affected by serious adverse events			
subjects affected / exposed	459 / 5976 (7.68%)	756 / 10259 (7.37%)	
number of deaths (all causes)	34	43	
number of deaths resulting from adverse events	34	43	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of the cervix			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix carcinoma			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system neoplasm			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Breast cancer recurrent			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm malignant			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign mesothelioma			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign hydatidiform mole			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Astrocytoma malignant			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cervix carcinoma stage 0			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Langerhans' cell histiocytosis			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric leiomyoma			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Female reproductive neoplasm			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial neoplasm			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ovarian neoplasm			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schwannoma			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine neuroendocrine tumour			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid neoplasm			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			

subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Lung neoplasm malignant			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia			
subjects affected / exposed	2 / 5976 (0.03%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 5976 (0.03%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial rupture			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial thrombosis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thrombophlebitis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superficial vein thrombosis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kawasaki's disease			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	5 / 5976 (0.08%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Abortion induced			

subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Haemorrhage in pregnancy			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HELLP syndrome			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gestational hypertension			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gestational diabetes			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion			
subjects affected / exposed	9 / 5976 (0.15%)	15 / 10259 (0.15%)	
occurrences causally related to treatment / all	0 / 9	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anembryonic gestation			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion threatened			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous incomplete			

subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion missed			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ectopic pregnancy			
subjects affected / exposed	2 / 5976 (0.03%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Threatened labour			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ruptured ectopic pregnancy			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature rupture of membranes			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature labour			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature delivery			
subjects affected / exposed	2 / 5976 (0.03%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pre-eclampsia			

subjects affected / exposed	5 / 5976 (0.08%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperemesis gravidarum			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous*			
subjects affected / exposed	4 / 5976 (0.07%)	14 / 10259 (0.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal death*			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	3 / 5976 (0.05%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 5976 (0.00%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Pyrexia			
subjects affected / exposed	0 / 5976 (0.00%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drowning			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ill-defined disorder			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodule			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Allergic oedema			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 5976 (0.00%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Substance abuser			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sexual abuse			

subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Physical assault			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Victim of homicide			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Reproductive system and breast disorders			
Testicular torsion			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular infarction			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Priapism			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst torsion			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst ruptured			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			

subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermenstrual bleeding			
subjects affected / exposed	7 / 5976 (0.12%)	5 / 10259 (0.05%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometriosis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysmenorrhoea			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast pain			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nasal polyps			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	4 / 5976 (0.07%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Bronchospasm			
subjects affected / exposed	1 / 5976 (0.02%)	5 / 10259 (0.05%)	
occurrences causally related to treatment / all	1 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthma			
subjects affected / exposed	9 / 5976 (0.15%)	20 / 10259 (0.19%)	
occurrences causally related to treatment / all	0 / 10	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			

subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	5 / 5976 (0.08%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumothorax spontaneous			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bipolar disorder			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety disorder			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aggression			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Depression			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic disorder			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	2 / 5976 (0.03%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatic symptom disorder			
subjects affected / exposed	2 / 5976 (0.03%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance abuse			
subjects affected / exposed	4 / 5976 (0.07%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance-induced psychotic disorder			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	9 / 5976 (0.15%)	10 / 10259 (0.10%)	
occurrences causally related to treatment / all	0 / 12	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	5 / 5976 (0.08%)	7 / 10259 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 2	0 / 1	
Contusion			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Craniofacial fracture			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder injury			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back injury			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 5976 (0.02%)	5 / 10259 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal bite			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Face injury			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hand fracture			

subjects affected / exposed	3 / 5976 (0.05%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
subjects affected / exposed	2 / 5976 (0.03%)	6 / 10259 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 2	0 / 2	
Fracture			
subjects affected / exposed	4 / 5976 (0.07%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body ingestion			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	3 / 5976 (0.05%)	5 / 10259 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	3 / 5976 (0.05%)	6 / 10259 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 5976 (0.03%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			

subjects affected / exposed	2 / 5976 (0.03%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	7 / 5976 (0.12%)	11 / 10259 (0.11%)	
occurrences causally related to treatment / all	0 / 7	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb fracture			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immunisation reaction			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	3 / 5976 (0.05%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	5 / 5976 (0.08%)	9 / 10259 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	2 / 5976 (0.03%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multiple injuries			
subjects affected / exposed	8 / 5976 (0.13%)	8 / 10259 (0.08%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 3	
Neck injury			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penetrating abdominal trauma			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poisoning			

subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 5976 (0.02%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 5976 (0.02%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin wound			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stab wound			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	3 / 5976 (0.05%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular injury			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	7 / 5976 (0.12%)	6 / 10259 (0.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 5976 (0.02%)	5 / 10259 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			

subjects affected / exposed	7 / 5976 (0.12%)	12 / 10259 (0.12%)	
occurrences causally related to treatment / all	0 / 7	0 / 12	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemothorax			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	3 / 5976 (0.05%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroschisis*			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syndactyly*			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	6 / 5976 (0.10%)	15 / 10259 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 17	
deaths causally related to treatment / all	0 / 2	0 / 3	

Angina pectoris			
subjects affected / exposed	2 / 5976 (0.03%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriospasm coronary			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Coronary artery disease			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 5976 (0.03%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			

Cerebellar stroke			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	6 / 5976 (0.10%)	8 / 10259 (0.08%)	
occurrences causally related to treatment / all	0 / 6	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bell's palsy			
subjects affected / exposed	2 / 5976 (0.03%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	4 / 5976 (0.07%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			

subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 5976 (0.00%)	5 / 10259 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Guillain-Barre syndrome			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Motor neurone disease			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial pressure increased			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoplegia			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Multiple sclerosis			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 5976 (0.02%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	6 / 5976 (0.10%)	9 / 10259 (0.09%)	
occurrences causally related to treatment / all	0 / 7	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ruptured cerebral aneurysm			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post herpetic neuralgia			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 5976 (0.02%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transverse sinus thrombosis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenia			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	5 / 5976 (0.08%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric lymphadenitis			
subjects affected / exposed	1 / 5976 (0.02%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 5976 (0.07%)	8 / 10259 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall haematoma			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bezoar			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen			
subjects affected / exposed	0 / 5976 (0.00%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia strangulated			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingival bleeding			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Internal hernia			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal perforation			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal prolapse			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic artery aneurysm			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	3 / 5976 (0.05%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	2 / 5976 (0.03%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	3 / 5976 (0.05%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	2 / 5976 (0.03%)	8 / 10259 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis fulminant			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cellulite			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin disorder			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			

subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petechiae			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Henoch-Schonlein purpura			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis bullous			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous vasculitis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephritic syndrome			
subjects affected / exposed	2 / 5976 (0.03%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			

subjects affected / exposed	11 / 5976 (0.18%)	13 / 10259 (0.13%)	
occurrences causally related to treatment / all	0 / 11	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	3 / 5976 (0.05%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anuria			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Choluria			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Glomerulonephritis acute			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis proliferative			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrotic syndrome			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post streptococcal glomerulonephritis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	2 / 5976 (0.03%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			

subjects affected / exposed	2 / 5976 (0.03%)	5 / 10259 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 5976 (0.05%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendonitis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			

subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess of eyelid			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
American trypanosomiasis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess jaw			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	26 / 5976 (0.44%)	45 / 10259 (0.44%)	
occurrences causally related to treatment / all	0 / 26	0 / 45	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bartholinitis			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 5976 (0.03%)	5 / 10259 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	35 / 5976 (0.59%)	51 / 10259 (0.50%)	
occurrences causally related to treatment / all	0 / 35	0 / 52	
deaths causally related to treatment / all	0 / 6	0 / 5	
COVID-19 pneumonia			
subjects affected / exposed	3 / 5976 (0.05%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cellulitis			
subjects affected / exposed	7 / 5976 (0.12%)	13 / 10259 (0.13%)	
occurrences causally related to treatment / all	0 / 7	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system infection			

subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chikungunya virus infection			
subjects affected / exposed	2 / 5976 (0.03%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus infection			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	14 / 5976 (0.23%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	2 / 15	0 / 4	
deaths causally related to treatment / all	1 / 1	0 / 0	
Dermatophytosis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous larva migrans			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	2 / 5976 (0.03%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fallopian tube abscess			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	12 / 5976 (0.20%)	24 / 10259 (0.23%)	
occurrences causally related to treatment / all	0 / 12	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIV infection			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious mononucleosis			

subjects affected / exposed	1 / 5976 (0.02%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis bacterial			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaria			
subjects affected / exposed	4 / 5976 (0.07%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinitis			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis herpes			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurocysticercosis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oophoritis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	1 / 5976 (0.02%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myiasis			
subjects affected / exposed	1 / 5976 (0.02%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal disease			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	5 / 5976 (0.08%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Puerperal infection			

subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary histoplasmosis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pelvic inflammatory disease			
subjects affected / exposed	3 / 5976 (0.05%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perichondritis			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal abscess			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	1 / 5976 (0.02%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	29 / 5976 (0.49%)	54 / 10259 (0.53%)	
occurrences causally related to treatment / all	0 / 32	0 / 58	
deaths causally related to treatment / all	0 / 1	0 / 2	
Pulmonary sepsis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	7 / 5976 (0.12%)	20 / 10259 (0.19%)	
occurrences causally related to treatment / all	0 / 9	0 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rickettsiosis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			

subjects affected / exposed	2 / 5976 (0.03%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Submandibular abscess			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sialoadenitis			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	5 / 5976 (0.08%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sporotrichosis			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Severe acute respiratory syndrome			

subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Suspected COVID-19			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular abscess			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 5976 (0.00%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	2 / 5976 (0.03%)	7 / 10259 (0.07%)	
occurrences causally related to treatment / all	0 / 2	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	11 / 5976 (0.18%)	25 / 10259 (0.24%)	
occurrences causally related to treatment / all	0 / 11	0 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	7 / 5976 (0.12%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			

subjects affected / exposed	1 / 5976 (0.02%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 5976 (0.00%)	5 / 10259 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 5976 (0.02%)	4 / 10259 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 5976 (0.02%)	0 / 10259 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 5976 (0.02%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 5976 (0.02%)	3 / 10259 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 5976 (0.00%)	2 / 10259 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 5976 (0.03%)	1 / 10259 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Dengue 1,2,3,4 (Attenuated) Vaccine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3112 / 5976 (52.07%)	6581 / 10259 (64.15%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1867 / 5976 (31.24%)	3772 / 10259 (36.77%)	
occurrences (all)	2824	5793	
General disorders and administration site conditions			
Administration site pruritus			
subjects affected / exposed	244 / 5976 (4.08%)	589 / 10259 (5.74%)	
occurrences (all)	271	657	
Administration site pain			
subjects affected / exposed	672 / 5976 (11.24%)	1536 / 10259 (14.97%)	
occurrences (all)	723	1652	
Chills			
subjects affected / exposed	336 / 5976 (5.62%)	886 / 10259 (8.64%)	
occurrences (all)	406	1005	
Fatigue			
subjects affected / exposed	914 / 5976 (15.29%)	1998 / 10259 (19.48%)	
occurrences (all)	1239	2756	
Pyrexia			
subjects affected / exposed	700 / 5976 (11.71%)	1580 / 10259 (15.40%)	
occurrences (all)	783	1762	
Eye disorders			
Photophobia			
subjects affected / exposed	488 / 5976 (8.17%)	1001 / 10259 (9.76%)	
occurrences (all)	648	1291	
Eye pain			
subjects affected / exposed	647 / 5976 (10.83%)	1639 / 10259 (15.98%)	
occurrences (all)	843	2058	
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	637 / 5976 (10.66%)	1258 / 10259 (12.26%)	
occurrences (all)	782	1568	
Vomiting			
subjects affected / exposed	300 / 5976 (5.02%)	582 / 10259 (5.67%)	
occurrences (all)	330	655	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	532 / 5976 (8.90%)	1980 / 10259 (19.30%)	
occurrences (all)	664	2347	
Rash			
subjects affected / exposed	254 / 5976 (4.25%)	2328 / 10259 (22.69%)	
occurrences (all)	274	2459	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	491 / 5976 (8.22%)	1165 / 10259 (11.36%)	
occurrences (all)	623	1501	
Myalgia			
subjects affected / exposed	768 / 5976 (12.85%)	1818 / 10259 (17.72%)	
occurrences (all)	1005	2320	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2017	The primary purpose of amendment 1 was to update the safety analysis, rationale for placebo use and include exploratory objective with regard to other arbovirus-related conditions.
08 April 2017	The primary purpose of amendment 2 was to incorporate authorization for use of the vaccine eight hours after reconstitution and update the safety information from the phase II study.
27 April 2018	The primary purpose of amendment 3 was to modify the subgroup of consistency of immune response to different lots of the vaccine.
19 June 2020	The primary purpose of amendment 4 was to clarify the time frame for performing unblinded interim analysis, specify type of nonstructural protein 1 analysis, add the possibility of using validated tests similar to the plaque reduction neutralization test and detail the arboviruses for evaluating interactions.
22 September 2021	The primary purpose of amendment 5 was to modify the immunological evaluation and revise evaluation times and sample size of the subgroup on consistency of immune response to different lots of the vaccine and incorporate a comparison of the conventional formulation and the simplified formulation.
22 September 2021	The primary purpose of amendment 6 was to make changes according to health agency requirements.
13 April 2022	The primary purpose of amendment 7 was to detail the center’s actions in the event it is contacted by the participant after the last protocol visit of the trial to report a serious adverse event or fever and adds rapid dengue testing for the inclusion of research participants.
20 April 2023	The primary purpose amendment 8 was to extend the mandatory contraception period by means of the use of an effective contraceptive method by 90 days post-vaccination and update the text on the estimated participant allocation by strata and study phases.
17 April 2024	The primary purpose of amendment 9 was to harmonize the objectives and endpoints previously described in the protocol, clarify that the sub-studies: Consistency of immune response to different lots of the vaccine and non-inferiority between the simplified formulation and the conventional formulations are described on Appendix C, and clarify that the mandatory contraception period by means of the use of an effective contraceptive method by 90 days post-vaccination is for the population of the lot consistency substudy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported