Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial to Investigate the Immunogenicity and Safety of Subcutaneous Administration of a Tetravalent Dengue Vaccine Candidate in Healthy Adolescent Subjects in Non-Endemic Area(s) for Dengue

Summary

EudraCT number	2018-003980-77
Trial protocol	Outside EU/EEA
Global end of trial date	26 January 2019

Results information

Result version number	v1 (current)
This version publication date	02 April 2020
First version publication date	02 April 2020

Trial information

Trial identification

Sponsor protocol code	DEN-315

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03341637
WHO universal trial number (UTN)	U1111-1192-7827

Notes:

Sponsors

Sponsor organisation name	Takeda Vaccines, Inc.
Sponsor organisation address	40 Landsdowne Street, Cambridge, United States, MA 02139
Public contact	Medical Director, Takeda Vaccines, Inc., +1 8778253327, trialdisclosures@takeda.com
Scientific contact	Medical Director, Takeda Vaccines, Inc., +1 8778253327, trialdisclosures@takeda.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001888-PIP01-15
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to describe the neutralizing antibody response against each dengue serotype at 1 month post second dose of TDV or placebo in dengue-naive adolescent participants.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 December 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Mexico: 400
Worldwide total number of subjects	400
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)	0
Adolescents (12-17 years)	400
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 5 investigative sites in Mexico from 14-Dec-2017 to 26-Jan-2019.

Pre-assignment

Screening details:

Healthy volunteers were enrolled in a 3:1 ratio into 2 parallel study groups: 1 study group received 2 doses of Tetravalent Dengue vaccine (TDV) and another group received 2 doses of TDV matching placebo subcutaneously (SC).

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

TDV placebo-matching 0.5 mL injection, subcutaneously, once on Day 0 (first dose) and Day 90 (second dose).

Arm type	Placebo
Investigational medicinal product name	Placebo- matching TDV injection
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Normal Saline (0.9% NaCl) subcutaneous injection

Arm title	Tetravalent Dengue Vaccine (TDV)

Arm description:

TDV 0.5 mL, injection, subcutaneously, once on Day 0 (first dose) and Day 90 (second dose).

Arm type	Experimental
Investigational medicinal product name	TDV injection
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

TDV subcutaneous injection

Number of subjects in period 1	Placebo	Tetravalent Dengue Vaccine (TDV)
Started	100	300
Completed	95	296
Not completed	5	4
Consent withdrawn by subject	3	3
Lost to follow-up	1	-
Reason not Specified	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
TDV placebo-matching 0.5 mL injection, subcutaneously, once on Day 0 (first dose) and Day 90 (second dose).	
Reporting group title	Tetravalent Dengue Vaccine (TDV)
Reporting group description:	
TDV 0.5 mL, injection, subcutaneously, once on Day 0 (first dose) and Day 90 (second dose).	

Reporting group values	Placebo	Tetravalent Dengue Vaccine (TDV)	Total
Number of subjects	100	300	400
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	100	300	400
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	14.3	14.3	
standard deviation	± 1.57	± 1.69	-
Sex: Female, Male Units: Subjects			
Female	51	176	227
Male	49	124	173
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	100	300	400
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	55	148	203
Multiracial	45	152	197
Region of Enrollment Units: Subjects			
Height Units: cm			
arithmetic mean	159.6	159.0	
standard deviation	± 8.94	± 8.68	-
Weight			

Units: kg			
arithmetic mean	57.60	56.84	
standard deviation	± 14.045	± 12.708	-
Body Mass Index (BMI)			
BMI=Weight/Height.			
Units: kg/m^2			
arithmetic mean	22.42	22.39	
standard deviation	± 4.237	± 4.266	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
TDV placebo-matching 0.5 mL injection, subcutaneously, once on Day 0 (first dose) and Day 90 (second dose).	
Reporting group title	Tetravalent Dengue Vaccine (TDV)
Reporting group description:	
TDV 0.5 mL, injection, subcutaneously, once on Day 0 (first dose) and Day 90 (second dose).	

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Day 120

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Day 120[1]
End point description:	
GMTs of neutralizing antibodies were measured by microneutralization test 50% [MNT50] for each of the 4 Dengue Serotypes. The 4 dengue virus serotypes were DENV-1, DENV-2, DENV-3 and DENV-4. Seropositivity is defined as reciprocal neutralizing titer ≥10. Per Protocol Set (PPS): all participants seronegative to all serotypes of dengue virus at baseline who received at least 1 dose of trial vaccine, who had a valid pre-dose (baseline) and at least 1 valid post-dose measurement for immunogenicity and no major protocol violations. n=participants with data available at given time-point.	
End point type	Primary
End point timeframe:	
One month post second dose (Day 120)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses was not available.

End point values	Placebo	Tetravalent Dengue Vaccine (TDV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	271		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1 (n=72, 243)	5.3 (4.7 to 5.8)	327.9 (281.7 to 381.8)		
DENV-2 (n=72, 243)	6.0 (5.2 to 7.0)	1742.5 (1522.6 to 1994.3)		
DENV-3 (n=72, 243)	5.2 (4.8 to 5.6)	119.5 (106.4 to 134.2)		
DENV-4 (n=72, 243)	5.1 (4.9 to 5.2)	142.7 (126.4 to 161.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Day 270

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Day 270

End point description:

GMTs of neutralizing antibodies were measured by microneutralization test 50% [MNT50] for each of the 4 Dengue Serotypes. The 4 dengue virus serotypes were DENV-1, DENV-2, DENV-3 and DENV-4. Seropositivity is defined as reciprocal neutralizing titer ≥10. PPS: all participants seronegative to all serotypes of dengue virus at baseline who received at least 1 dose of trial vaccine, who had a valid pre-dose (baseline) and at least 1 valid post-dose measurement for immunogenicity and no major protocol violations. n=participants with data available at given time-point. 99999 indicates data for 95% CI was not evaluable at this time point.

End point type	Secondary

End point timeframe:

Six months post second dose (Day 270)

End point values	Placebo	Tetravalent Dengue Vaccine (TDV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	271		
Units: titer				
geometric mean (standard deviation)				
DENV-1 (n=73, 254)	5.4 (± 1.58)	134.7 (± 3.73)		
DENV-2 (n= 73, 254)	5.2 (± 1.30)	740.9 (± 3.06)		
DENV-3 (n=73, 254)	5.3 (± 1.49)	45.8 (± 2.59)		
DENV-4 (n=73, 254)	5.0 (± 1.00)	37.5 (± 2.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Seropositivity Rates for Each of the 4 Dengue Serotypes

End point title	Seropositivity Rates for Each of the 4 Dengue Serotypes

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, was derived from the titers of dengue-neutralizing antibodies. Seropositivity defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes were DENV-1, DENV-2, DENV-3 and DENV-4. PPS: all participants seronegative to all serotypes of dengue virus at baseline who received at least 1 dose of trial vaccine, who had a valid pre-dose (baseline) and at least 1 valid post-dose measurement for immunogenicity and no major protocol violations. n= participants with data available at given time-point.

End point type	Secondary

End point timeframe:

One month and six months post second dose (Day 120 and Day 270)

End point values	Placebo	Tetravalent Dengue Vaccine (TDV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	271		
Units: percentage of participants				
number (confidence interval 95%)				
Day 120 (Month 4): DENV-1 (n=72,243)	1.4 (0.0 to 7.5)	100.0 (98.5 to 100.0)		
Day 120 (Month 4): DENV-2 (n=72,243)	8.3 (3.1 to 17.3)	100.0 (98.5 to 100.0)		
Day 120 (Month 4): DENV-3 (n=72,243)	1.4 (0.0 to 7.5)	100.0 (98.5 to 100.0)		
Day 120 (Month 4): DENV-4 (n=72,243)	1.4 (0.0 to 7.5)	99.6 (97.7 to 100.0)		
Day 270 (Month 9): DENV-1 (n=73,254)	2.7 (0.3 to 9.5)	98.4 (96.0 to 99.6)		
Day 270 (Month 9): DENV-2 (n=73,254)	1.4 (0.0 to 7.4)	99.6 (97.8 to 100.0)		
Day 270 (Month 9): DENV-3 (n=73,254)	2.7 (0.3 to 9.5)	92.1 (88.1 to 95.1)		
Day 270 (Month 9): DENV-4 (n=73,254)	0 (0.0 to 4.9)	89.4 (84.9 to 92.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Seropositivity Rates for Multiple (2, 3 or 4) Dengue Serotypes

End point title	Seropositivity Rates for Multiple (2, 3 or 4) Dengue Serotypes

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, was derived from the titers of dengue-neutralizing antibodies. Seropositivity was defined as a reciprocal neutralizing titer ≥10. PPS: all participants seronegative to all serotypes of dengue virus at baseline who received at least 1 dose of trial vaccine, who had a valid pre-dose (baseline) and at least 1 valid post-dose measurement for immunogenicity and no major protocol violations. n= participants with data available at given time-point.

End point type	Secondary

End point timeframe:

One month and six months post second dose (Day 120 and Day 270)

End point values	Placebo	Tetravalent Dengue Vaccine (TDV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	271		
Units: percentage of participants				
number (confidence interval 95%)				
Day 120 (Month 4): At Least Bivalent (n=72, 243)	1.4 (0.0 to 7.5)	100.0 (98.5 to 100.0)		
Day 120 (Month 4): At Least Trivalent (n=72, 243)	1.4 (0.0 to 7.5)	100.0 (98.5 to 100.0)		

Day 120 (Month 4): Tetravalent (n=72, 243)	1.4 (0.0 to 7.5)	99.6 (97.7 to 100.0)		
Day 270 (Month 9): At Least Bivalent (n=73, 254)	0 (0.0 to 4.9)	99.2 (97.2 to 99.9)		
Day 270 (Month 9): At Least Trivalent (n=73, 254)	0 (0.0 to 4.9)	94.5 (90.9 to 97.0)		
Day 270 (Month 9): Tetravalent (n=73, 254)	0 (0.0 to 4.9)	85.8 (80.9 to 89.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Solicited Local (Injection Site) Adverse Events (AEs) (Diary Recorded) Following Each Vaccination by Severity

End point title	Percentage of Participants with Solicited Local (Injection Site) Adverse Events (AEs) (Diary Recorded) Following Each Vaccination by Severity

End point description:

Solicited local AEs (at injection site) were collected by participants using diary cards within 7 days after vaccination (Vac.) and included pain (none, mild: no interference with daily activity, moderate: interference with daily activity with or without treatment and severe: prevents daily activity with or without treatment), redness (erythema) (<2.5 cm, mild: 2.5-5 cm, moderate: >5 to <=10 cm, severe: >10 cm) and swelling (edema/induration) (<2.5 cm, mild: 2.5-5 cm, moderate: >5 to <=10 cm, severe: >10 cm). Safety Set included of all participants who received at least 1 dose of trial vaccine. Number analyzed is the number of participants with data available at the given timepoint. Only categories for which there was at least 1 participant are reported. n=participants with data available for given category. First vaccination= 1st vac.; Second vaccination=2nd vac.

End point type	Secondary

End point timeframe:

Within 7 days after each vaccination

End point values	Placebo	Tetravalent Dengue Vaccine (TDV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	300		
Units: percentage of participants				
number (not applicable)				
After First Vaccination (Vac.),Any AEs(n=99,299)	34.3	56.2		
After First Vac., Pain:Mild (n=99, 299)	26.3	44.8		
After First Vac., Pain:Moderate (n=99, 299)	7.1	9.7		
After First Vac., Pain:Severe (n=99, 299)	1.0	0.7		
After First Vac., Erythema:Mild (n=99, 299)	0	5.7		
After First Vac., Swelling:Mild (n=99, 299)	0	4.3		
After Second Vac.,Any AEs(n=94,295)	30.9	52.2		
After Second Vac., Pain:Mild (n=94, 295)	24.5	35.6		

After Second Vac., Pain:Moderate(n=94,295)	5.3	13.2		
After Second Vac., Pain:Severe (n=94, 295)	1.1	3.1		
After Second Vac., Erythema:Mild(n=94,295)	0	4.1		
After Second Vac., Swelling:Mild(n=100,300)	0	1.7		
After Second Vac., Swelling:Moderate(n=100,300)	0	0.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Solicited Systemic Adverse Events (AEs) (Diary Recorded) Following Each Vaccination by Severity

End point title	Percentage of Participants with Solicited Systemic Adverse Events (AEs) (Diary Recorded) Following Each Vaccination by Severity

End point description:

Solicited systemic AEs were collected by participants using diary cards within 14 days after vaccination and included fever, headache, tiredness or weakness (asthenia), feeling of discomfort (malaise) and muscle pain (myalgia). Severity scales for headache:none, mild:no interference with daily activity, moderate:interference with daily activity with or without treatment and severe:prevents normal activity with/without treatment. Severity scales for others:none, mild:no interference with daily activity, moderate:interference with daily activity and severe: prevents daily activity. systemic AE of fever (i.e. ≥38°C or ≥100.4°F) was derived from daily temperature reading recorded within 14 days after vaccination. Fever was excluded from overall count as no severity grading was applied for it. Safety Set:participants who received at least 1 dose of trial vaccine.Only categories for which there was at least 1 participant are reported. n= participants with data available for given category.

End point type	Secondary

End point timeframe:

Within 14 days after each vaccination

End point values	Placebo	Tetravalent Dengue Vaccine (TDV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	300		
Units: percentage of participants				
number (not applicable)				
After First Vaccination(Vac.): Any (n=99, 299)	58.6	66.6		
After First Vac.: Headache-Mild (n=99, 299)	25.3	31.4		
After First Vac.:Headache-Moderate(n=99,299)	18.2	10.4		
After First Vac.:Headache-Severe(n=99,299)	1.0	2.7		
After First Vac.:Asthenia-Mild (n=99,299)	20.2	24.7		
After First Vac.:Asthenia-Moderate(n=99,299)	13.1	7.7		

After First Vac.: Asthenia-Severe(n=99,299)	2.0	2.3		
After First Vac.: Malaise-Mild (n=99,299)	20.2	18.7		
After First Vac.:Malaise-Moderate(n=99,299)	11.1	7.7		
After First Vac.:Malaise-Severe(n=99,299)	2.0	1.3		
After First Vac.:Myalgia-Mild (n=99,299)	26.3	36.1		
After First Vac.:Myalgia-Moderate(n=99,299)	13.1	10.7		
After First Vac.:Myalgia-Severe(n=99,299)	1.0	1.0		
After 1st Vaccination:Fever-Any (n=100,300)	5.1	6.7		
After First Vac.:Fever(38-<38.5°C)(n=99,299)	3.0	3.0		
After First Vac.:Fever (38.5-<39°C)(n=99,299)	2.0	2.3		
After First Vac.:Fever(39-<39.5°C)(n=99,299)	0.0	1.0		
After First Vac.:Fever (39.5-<40°C)(n=99,299)	0.0	0.3		
After Second Vac: Any (n=94,296)	45.7	49.3		
After Second Vac: Headache-Mild (n=94,296)	20.2	24.3		
After Second Vac.:Headache-Moderate(n=94,296)	6.4	8.4		
After Second Vac.:Headache-Severe(n=94,296)	3.2	2.7		
After Second Vac.:Asthenia-Mild(n=94,296)	22.3	19.9		
After Second Vac.:Asthenia-Moderate(n=94,296)	4.3	6.8		
After Second Vac.:Asthenia-Severe(n=94,296)	1.1	1.4		
After Second Vac.:Malaise-Mild(n=94,296)	12.8	16.2		
After Second Vac.:Malaise-Moderate(n=94,296)	6.4	5.1		
After Second Vac.:Malaise-Severe(n=94,296)	4.3	2.4		
After Second Vac.:Myalgia-Mild(n=94,296)	21.3	25.7		
After Second Vac.:Myalgia-Moderate(n=94,296)	8.5	6.8		
After Second Vac.:Myalgia-Severe(n=94,296)	1.1	2.4		
After Second Vac.:Fever-Any(n=100,300)	3.2	6.8		
After Second Vac.:Fever(38-<38.5°C)(n=94,296)	1.1	3.7		
After Second Vac.:Fever(38.5-<39°C)(n=94,296)	1.1	2.0		
After Second Vac.:Fever(39-<39.5°C)(n=100,300)	1.1	0.7		
After Second Vac.:Fever(39.5-<40°C)(n=100,300)	0.0	0.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with any Unsolicited Adverse Events (AEs) Following Each Vaccination

End point title	Percentage of Participants with any Unsolicited Adverse Events (AEs) Following Each Vaccination

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. Safety Set included of all participants who received at least 1 dose of trial vaccine. Number analyzed is the number of participants with data available at the given timepoint. Only categories for which there was at least 1 participant are reported. n= participants with data available for given category.

End point type	Secondary

End point timeframe:

Within 28 days after each vaccination

End point values	Placebo	Tetravalent Dengue Vaccine (TDV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	300		
Units: percentage of participants				
number (not applicable)				
After First Vaccination (n=100, 300)	25.0	30.0		
After Second Vaccination (n=95, 297)	17.9	23.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Medically Attended AEs (MAAEs) Throughout the Study

End point title	Percentage of Participants with Medically Attended AEs (MAAEs) Throughout the Study

End point description:

MAAEs were defined as AEs leading to a medical visit to or by a healthcare professional including visits to an emergency department, but not fulfilling seriousness criteria. Safety Set included of all participants who received at least 1 dose of trial vaccine.

End point type	Secondary

End point timeframe:

From first vaccination (Day 1) through end of study (Day 270)

End point values	Placebo	Tetravalent Dengue Vaccine (TDV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	300		
Units: percentage of participants				
number (not applicable)	38.0	47.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Serious Adverse Events (SAEs) Throughout the Study

End point title	Percentage of Participants with Serious Adverse Events (SAEs) Throughout the Study

End point description:

An SAE was defined as any untoward medical occurrence or effect that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or is medically important due to other reasons than the above mentioned criteria. Safety Set included of all participants who received at least 1 dose of trial vaccine.

End point type	Secondary

End point timeframe:

From first vaccination (Day 1) through end of study (Day 270)

End point values	Placebo	Tetravalent Dengue Vaccine (TDV)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	300		
Units: percentage of participants				
number (not applicable)	2.0	0.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events: Within 28 days of Vaccination; Serious adverse events (SAEs): From first vaccination (Day 1) through end of study (Day 270)

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

TDV placebo-matching 0.5 mL injection, subcutaneously, once on Day 0 (first dose) and Day 90 (second dose).

Reporting group title	Tetravalent Dengue Vaccine (TDV)

Reporting group description:

TDV 0.5 mL, injection, subcutaneously, once on Day 0 (first dose) and Day 90 (second dose).

Serious adverse events	Placebo	Tetravalent Dengue Vaccine (TDV)	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 100 (2.00%)	1 / 300 (0.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 100 (1.00%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			

subjects affected / exposed	1 / 100 (1.00%)	0 / 300 (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	0 / 100 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo	Tetravalent Dengue Vaccine (TDV)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 100 (38.00%)	112 / 300 (37.33%)	
Nervous system disorders			
Syncope			
subjects affected / exposed	2 / 100 (2.00%)	9 / 300 (3.00%)	
occurrences (all)	2	10	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	3 / 100 (3.00%)	7 / 300 (2.33%)	
occurrences (all)	3	7	
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	14 / 100 (14.00%)	43 / 300 (14.33%)	
occurrences (all)	17	47	
Nasopharyngitis			
subjects affected / exposed	6 / 100 (6.00%)	24 / 300 (8.00%)	
occurrences (all)	6	25	
Viral pharyngitis			
subjects affected / exposed	7 / 100 (7.00%)	15 / 300 (5.00%)	
occurrences (all)	7	15	
Pharyngitis			
subjects affected / exposed	4 / 100 (4.00%)	10 / 300 (3.33%)	
occurrences (all)	4	10	
Pharyngitis bacterial			

subjects affected / exposed	2 / 100 (2.00%)	9 / 300 (3.00%)	
occurrences (all)	2	9	
Gastroenteritis			
subjects affected / exposed	2 / 100 (2.00%)	8 / 300 (2.67%)	
occurrences (all)	2	8	
Upper respiratory tract infection bacterial			
subjects affected / exposed	1 / 100 (1.00%)	9 / 300 (3.00%)	
occurrences (all)	1	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported