Clinical trial results:
A Phase II, Double-Blind, Controlled Trial to Assess the Safety and Immunogenicity of Different Schedules of Takeda's Tetravalent Dengue Vaccine Candidate (TDV) in Healthy Subjects Aged Between 2 and <18 Years and Living in Dengue Endemic Countries in Asia and Latin America

Summary

EudraCT number	2018-003978-28
Trial protocol	Outside EU/EEA
Global end of trial date	18 February 2019

Results information

Result version number	v1 (current)
This version publication date	26 February 2020
First version publication date	26 February 2020

Trial information

Trial identification

Sponsor protocol code	DEN-204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02302066
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	Takeda Vaccines, Inc., 40 Landsdowne Street Cambridge, MA, United States, United States, 02139
Public contact	Medical Director, Takeda, +1 877-825-3327, clinicaltrialregistry@tpna.com
Scientific contact	Medical Director, Takeda, +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	18 February 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to assess the humoral immune responses to Takeda's Tetravalent Dengue Vaccine Candidate (TDV) administered subcutaneously in a subset of healthy participants between 2 and <18 years of age living in dengue endemic countries.

Protection of trial subjects:

All study subjects or their guardians were required to read and sign an Informed Consent Form

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 December 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Dominican Republic: 535
Country: Number of subjects enrolled	Panama: 935
Country: Number of subjects enrolled	Philippines: 330
Worldwide total number of subjects	1800
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)	1463
Adolescents (12-17 years)	337
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 3 investigative sites in Dominican Republic, Panama and Philippines from 05 Dec 2014 to 18 Feb 2019.

Pre-assignment

Screening details:

Healthy volunteers were enrolled in a 1:2:5:1 ratio into 4 study groups: Group 1 received two doses of Tetravalent Dengue Vaccine (TDV), Group 2 received one dose of TDV, Group 3 received one dose of TDV along with booster vaccination and Group 4 received placebo.

Pre-assignment period milestones

Number of subjects started	1800
Number of subjects completed	1794

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Randomized but not Treated: 6

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, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 (TDV 2-Dose)

Arm description:

Takeda's tetravalent dengue vaccine candidate (TDV), 0.5 mL, subcutaneous injection on Days 1 and 91. Placebo-matching, 0.5 mL, subcutaneous injection on Day 365.

Arm type	Experimental
Investigational medicinal product name	Takeda's tetravalent dengue vaccine candidate (TDV)
Investigational medicinal product code	
Other name	DenVax
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Takeda's tetravalent dengue vaccine candidate (TDV), 0.5 mL, subcutaneous injection on Days 1 and 91.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo-matching, 0.5 mL, subcutaneous injection on Day 365.

Arm title	Group 2 (TDV 1-Dose)

Arm description:

Takeda's TDV, 0.5 mL, subcutaneous injection on Day 1. Placebo-matching, 0.5 mL, subcutaneous

injection on Days 91 and 365.

Arm type	Experimental
Investigational medicinal product name	Takeda\'s tetravalent dengue vaccine candidate (TDV)
Investigational medicinal product code	
Other name	DenVax
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Takeda's tetravalent dengue vaccine candidate (TDV), 0.5 mL, subcutaneous injection on Days 1.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo-matching, 0.5 mL, subcutaneous injection on Days 91 and 365.

Arm title	Group 3 (TDV 1-Dose + Booster)

Arm description:

Takeda's TDV, 0.5 mL, subcutaneous injection on Days 1 and 365. Placebo-matching, 0.5 mL, subcutaneous injection on Day 91.

Arm type	Experimental
Investigational medicinal product name	Takeda\'s tetravalent dengue vaccine candidate (TDV)
Investigational medicinal product code	
Other name	DenVax
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Takeda's tetravalent dengue vaccine candidate (TDV), 0.5 mL, subcutaneous injection on Days 1 and 365.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo-matching, 0.5 mL, subcutaneous injection on Day 91.

Arm title	Group 4 (Placebo Control)

Arm description:

Placebo-matching, 0.5 mL, subcutaneous injection on Days 1, 91 and 365.

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

Dosage and administration details:

Placebo-matching, 0.5 mL, subcutaneous injection on Day 1, 91 and 365

Number of subjects in period 1[1]	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 3 (TDV 1-Dose + Booster)
Started	200	398	998
Immunogenicity Subset	92 [2]	187 [3]	192 [4]
Per-Protocol Set (PPS)	83 [5]	171 [6]	174 [7]
Completed	192	376	954
Not completed	8	22	44
Adverse Event	2	1	4
Reason Not Specified	-	1	5
Pregnancy	-	4	-
Withdrawal by Subject	5	15	27
Lost to follow-up	1	1	8

Number of subjects in period 1[1]	Group 4 (Placebo Control)
Started	198
Immunogenicity Subset	94 [8]
Per-Protocol Set (PPS)	81 [9]
Completed	187
Not completed	11
Adverse Event	-
Reason Not Specified	2
Pregnancy	-
Withdrawal by Subject	5
Lost to follow-up	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: This is based on Safety Set.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is Per-protocol Set.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is Per-protocol Set.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is Per-protocol Set.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is Per-protocol Set.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that

completed, minus those who left.

Justification: This is Per-protocol Set.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This is Per-protocol Set.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This is Per-protocol Set.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This is Per-protocol Set.

Baseline characteristics

Reporting groups	
Reporting group title	Group 1 (TDV 2-Dose)
Reporting group description:	
Takeda's tetravalent dengue vaccine candidate (TDV), 0.5 mL, subcutaneous injection on Days 1 and 91. Placebo-matching, 0.5 mL, subcutaneous injection on Day 365.	
Reporting group title	Group 2 (TDV 1-Dose)
Reporting group description:	
Takeda's TDV, 0.5 mL, subcutaneous injection on Day 1. Placebo-matching, 0.5 mL, subcutaneous injection on Days 91 and 365.	
Reporting group title	Group 3 (TDV 1-Dose + Booster)
Reporting group description:	
Takeda's TDV, 0.5 mL, subcutaneous injection on Days 1 and 365. Placebo-matching, 0.5 mL, subcutaneous injection on Day 91.	
Reporting group title	Group 4 (Placebo Control)
Reporting group description:	
Placebo-matching, 0.5 mL, subcutaneous injection on Days 1, 91 and 365.	

Reporting group values	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 3 (TDV 1-Dose + Booster)
Number of subjects	200	398	998
Age categorical Units: Subjects			
Children (2-11 years)	162	323	811
Adolescents (12-17 years)	38	75	187
Age Continuous Units: years			
arithmetic mean	7.3	7.3	7.3
standard deviation	± 4.01	± 4.14	± 4.06
Sex: Female, Male Units: Subjects			
Female	100	207	486
Male	100	191	512
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	165	317	825
Not Hispanic or Latino	35	81	173
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	102	204	505
Asian	35	82	174
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	63	110	311
White	0	2	8
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Height			
Units: cm			
arithmetic mean	122.1	120.9	121.4
standard deviation	± 22.59	± 23.15	± 22.60
Weight			
Units: kg			
arithmetic mean	27.86	27.25	27.12
standard deviation	± 15.069	± 14.368	± 13.612
Body Mass Index (BMI)			
Body Mass Index=weight/[height^2]			
Units: kg/m^2			
arithmetic mean	17.42	17.43	17.29
standard deviation	± 3.558	± 3.306	± 3.123

Reporting group values	Group 4 (Placebo Control)	Total	
Number of subjects	198	1794	
Age categorical			
Units: Subjects			
Children (2-11 years)	162	1458	
Adolescents (12-17 years)	36	336	
Age Continuous			
Units: years			
arithmetic mean	7.0		
standard deviation	± 3.96	-	
Sex: Female, Male			
Units: Subjects			
Female	95	888	
Male	103	906	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	158	1465	
Not Hispanic or Latino	40	329	
Unknown or Not Reported	0	0	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	101	912	
Asian	40	331	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	56	540	
White	1	11	
More than one race	0	0	
Unknown or Not Reported	0	0	
Height			
Units: cm			
arithmetic mean	119.3		
standard deviation	± 21.88	-	
Weight			
Units: kg			
arithmetic mean	25.66		
standard deviation	± 13.371	-	

Body Mass Index (BMI)			
Body Mass Index=weight/[height^2]			
Units: kg/m^2			
arithmetic mean	16.93		
standard deviation	± 2.975	-	

End points

End points reporting groups

Reporting group title	Group 1 (TDV 2-Dose)
Reporting group description:	
Takeda's tetravalent dengue vaccine candidate (TDV), 0.5 mL, subcutaneous injection on Days 1 and 91. Placebo-matching, 0.5 mL, subcutaneous injection on Day 365.	
Reporting group title	Group 2 (TDV 1-Dose)
Reporting group description:	
Takeda's TDV, 0.5 mL, subcutaneous injection on Day 1. Placebo-matching, 0.5 mL, subcutaneous injection on Days 91 and 365.	
Reporting group title	Group 3 (TDV 1-Dose + Booster)
Reporting group description:	
Takeda's TDV, 0.5 mL, subcutaneous injection on Days 1 and 365. Placebo-matching, 0.5 mL, subcutaneous injection on Day 91.	
Reporting group title	Group 4 (Placebo Control)
Reporting group description:	
Placebo-matching, 0.5 mL, subcutaneous injection on Days 1, 91 and 365.	
Subject analysis set title	Group 1 (TDV 2-Dose) Infant/Toddler
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants aged <6 years received Takeda's tetravalent dengue vaccine candidate (TDV), 0.5 mL, subcutaneous injection on Days 1 and 91. Placebo matching, 0.5 mL, subcutaneous injection on Day 365.	
Subject analysis set title	Group 2 (TDV 1-Dose) Infant/Toddler
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants aged <6 years received Takeda's TDV, 0.5 mL, subcutaneous injection on Day 1. Placebo matching, 0.5 mL, subcutaneous injection on Days 91 and 365.	
Subject analysis set title	Group 3 (TDV 2-Dose) Infant/Toddler
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants aged <6 years received Takeda's TDV, 0.5 mL, subcutaneous injection on Days 1 and 365. Placebo matching, 0.5 mL, subcutaneous injection on Day 91.	
Subject analysis set title	Group 4 (Placebo Control) Infant/Toddler
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants aged <6 years received placebo matching, 0.5 mL, subcutaneous injection on Days 1, 91 and 365.	
Subject analysis set title	Group 1 (TDV 2-Dose) Adult/Children
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants aged ≥6 years received Takeda's tetravalent dengue vaccine candidate (TDV), 0.5 mL, subcutaneous injection on Days 1 and 91. Placebo matching, 0.5 mL, subcutaneous injection on Day 365.	
Subject analysis set title	Group 2 (TDV 1-Dose) Adult/Children
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants aged ≥6 years received Takeda's TDV, 0.5 mL, subcutaneous injection on Day 1. Placebo matching, 0.5 mL, subcutaneous injection on Days 91 and 365.	
Subject analysis set title	Group 3 (TDV 1-Dose + Booster) Adult/Children
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants aged ≥6 years received Takeda's TDV, 0.5 mL, subcutaneous injection on Days 1 and 365.	

Placebo matching, 0.5 mL, subcutaneous injection on Day 91.

Subject analysis set title	Group 4 (Placebo Control) Adult/Children
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participant aged ≥6 years received placebo matching, 0.5 mL, subcutaneous injection on Days 1, 91 and 365.

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies (Microneutralization Test [MNT50]) for Each of the Four DENV Serotypes for Participants in the Immunogenicity Subset.

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies (Microneutralization Test [MNT50]) for Each of the Four DENV Serotypes for Participants in the Immunogenicity Subset.[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. PPS: All participants who received at least 1 dose of trial vaccine, who had a valid pre-dose and at least 1 valid post-dose measurement for immunogenicity and no major protocol violations. PPS included only participants from Immunogenicity Subset. 'n' indicates number analyzed are participants with data available at the given timepoint. Data reported for up to Month 48 was collected at Months 1, 3, 6, 12, 13, 18, 24, 36 and 48.

End point type	Primary

End point timeframe:

Up to Month 48

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 is not available for this endpoint.

End point values	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 3 (TDV 1-Dose + Booster)	Group 4 (Placebo Control)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	83	171	174	81
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1, Day 28 (Month 1),n=83,171,174,81	768.2 (498.7 to 1183.4)	999.7 (723.6 to 1381.2)	920.9 (689.4 to 1230.1)	60.7 (31.8 to 116.0)
DENV-2, Day 28 (Month 1),n=83,171,174,81	4329.7 (2847.6 to 6583.2)	4219.3 (3118.9 to 5708.1)	3572.2 (2674.6 to 4771.2)	75.0 (39.6 to 141.8)
DENV-3, Day 28 (Month 1),n=83,171,174,81	216.1 (124.7 to 374.6)	352.8 (237.5 to 524.2)	363.6 (249.8 to 529.1)	45.8 (25.9 to 81.1)
DENV-4, Day 28 (Month 1),n=83,171,174,81	199.2 (130.0 to 305.2)	317.3 (232.2 to 433.5)	260.4 (195.0 to 347.7)	24.8 (16.2 to 38.0)
DENV-1, Day 91 (Month 3),n=83,171,174,81	422.3 (256.7 to 695.0)	684.2 (491.4 to 952.8)	708.9 (522.6 to 961.6)	64.6 (33.8 to 123.4)
DENV-2, Day 91 (Month 3),n=83,171,174,81	1810.1 (1311.1 to 2499.2)	2216.9 (1750.8 to 2807.2)	1709.6 (1370.4 to 2132.7)	76.0 (40.1 to 144.3)
DENV-3, Day 91 (Month 3),n=83,171,174,81	140.8 (83.8 to 236.6)	250.8 (174.5 to 360.6)	251.9 (175.7 to 361.2)	39.3 (22.6 to 68.2)
DENV-4, Day 91 (Month 3),n=83,171,174,81	122.9 (77.6 to 194.6)	170.8 (122.6 to 237.8)	147.0 (108.4 to 199.2)	23.4 (14.9 to 36.9)
DENV-1, Day 180 (Month 6),n=83,170,174,81	448.8 (293.0 to 687.5)	463.7 (329.5 to 652.6)	538.9 (391.2 to 742.3)	55.7 (29.2 to 106.6)
DENV-2, Day 180 (Month 6),n=83,170,174,81	1461.5 (1071.7 to 1992.9)	1682.9 (1333.5 to 2124.0)	1335.1 (1067.7 to 1669.5)	77.2 (39.8 to 149.6)

DENV-3, Day 180 (Month 6),n=83,170,174,81	150.1 (96.9 to 232.6)	166.3 (117.6 to 235.3)	173.9 (125.8 to 240.5)	37.4 (21.7 to 64.6)
DENV-4, Day 180 (Month 6),n=83,170,174,81	109.1 (72.9 to 163.2)	110.0 (81.0 to 149.2)	92.3 (68.7 to 123.9)	22.3 (14.1 to 35.1)
DENV-1, Day 365 (Month 12),n=79,161,164,76	370.7 (232.3 to 591.8)	409.6 (287.9 to 582.5)	487.3 (346.2 to 686.0)	72.7 (38.0 to 139.1)
DENV-2, Day 365 (Month 12),n=79,161,164,76	1070.0 (746.7 to 1533.2)	1529.8 (1179.0 to 1985.0)	1041.0 (802.8 to 1349.9)	133.9 (67.7 to 264.9)
DENV-3, Day 365 (Month 12),n=79,161,164,76	166.8 (101.4 to 274.2)	201.0 (139.0 to 290.4)	199.2 (138.7 to 286.1)	62.0 (34.6 to 111.0)
DENV-4, Day 365 (Month 12),n=79,161,164,76	87.9 (57.7 to 133.8)	85.6 (63.0 to 116.3)	89.3 (64.5 to 123.6)	29.3 (18.5 to 46.6)
DENV-1, Day 393 (Month 13),n=80,163,167,75	454.4 (273.4 to 755.2)	385.8 (271.6 to 548.2)	1598.8 (1258.2 to 2031.6)	80.6 (41.4 to 156.9)
DENV-2, Day 393 (Month 13),n=80,163,167,75	1152.4 (796.3 to 1667.6)	1384.1 (1066.3 to 1796.7)	1866.1 (1551.4 to 2244.6)	129.5 (64.9 to 258.6)
DENV-3, Day 393 (Month 13),n=80,163,167,75	192.1 (115.3 to 320.3)	225.1 (157.1 to 322.7)	767.6 (615.4 to 957.4)	68.5 (36.5 to 128.8)
DENV-4, Day 393 (Month 13),n=80,163,167,75	90.5 (58.1 to 141.2)	86.3 (64.2 to 116.1)	278.0 (226.6 to 340.9)	28.8 (18.0 to 46.0)
DENV-1, Day 540 (Month 18),n=81,168,172,80	475.9 (286.3 to 791.0)	461.3 (329.1 to 646.6)	1056.3 (804.0 to 1387.9)	92.2 (49.1 to 172.9)
DENV-2, Day 540 (Month 18),n=81,168,172,80	1211.5 (841.6 to 1744.1)	1241.8 (947.1 to 1628.1)	1456.6 (1181.7 to 1795.5)	176.7 (92.8 to 336.7)
DENV-3, Day 540 (Month 18),n=81,168,172,80	285.5 (170.7 to 477.5)	298.0 (205.0 to 433.3)	548.0 (411.2 to 730.3)	77.6 (44.0 to 136.9)
DENV-4, Day 540 (Month 18),n=81,168,172,80	98.3 (64.5 to 149.9)	102.0 (75.1 to 138.6)	171.6 (132.9 to 221.6)	33.1 (21.1 to 51.9)
DENV-1, Day 730 (Month 24),n=71,145,148,70	471.1 (289.9 to 765.4)	441.5 (302.4 to 644.3)	920.9 (699.9 to 1211.8)	114.5 (58.8 to 223.0)
DENV-2, Day 730 (Month 24),n=71,145,148,70	1395.5 (962.1 to 2024.3)	1748.2 (1328.8 to 2300.0)	1685.8 (1346.1 to 2111.3)	244.6 (118.2 to 506.3)
DENV-3, Day 730 (Month 24),n=71,145,148,70	243.0 (144.2 to 409.3)	276.0 (188.3 to 404.7)	470.1 (347.7 to 635.7)	90.8 (46.6 to 176.8)
DENV-4, Day 730 (Month 24),n=71,145,148,70	180.0 (113.5 to 285.6)	170.4 (121.3 to 239.4)	285.9 (219.6 to 372.1)	56.3 (32.1 to 98.9)
DENV-1, Day 1095 (Month 36)n=66,137,139,66	495.2 (278.9 to 879.3)	364.7 (246.3 to 540.1)	742.8 (553.6 to 996.8)	90.7 (47.3 to 173.7)
DENV-2, Day 1095 (Month 36),n=66,137,139,66	1394.2 (946.4 to 2053.9)	1408.4 (1057.3 to 1876.0)	1476.2 (1153.3 to 1889.7)	203.5 (100.0 to 414.0)
DENV-3, Day 1095 (Month 36),n=66,137,139,66	262.8 (158.2 to 436.5)	214.9 (144.5 to 319.7)	364.8 (266.4 to 499.4)	66.4 (35.1 to 125.5)
DENV-4, Day 1095 (Month 36),n=66,137,139,66	201.8 (125.2 to 325.3)	148.1 (104.8 to 209.3)	236.1 (179.4 to 310.6)	45.7 (27.0 to 77.2)
DENV-1, Day 1460 (Month 48),n=65,133,136,63	377.8 (226.1 to 631.5)	421.0 (285.1 to 621.9)	718.5 (537.7 to 959.9)	100.0 (49.8 to 200.7)
DENV-2, Day 1460 (Month 48),n=65,133,136,63	1051.9 (732.2 to 1511.1)	1319.0 (970.1 to 1793.5)	1200.0 (927.1 to 1553.1)	208.1 (99.2 to 436.5)
DENV-3, Day 1460 (Month 48),n=65,133,136,63	183.4 (112.9 to 298.0)	200.5 (135.1 to 297.6)	287.5 (210.7 to 392.4)	71.3 (36.6 to 138.9)
DENV-4, Day 1460 (Month 48),n=65,133,136,63	152.0 (96.6 to 239.2)	164.1 (114.1 to 236.0)	218.6 (164.7 to 290.2)	46.2 (26.1 to 81.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Seropositivity Rates For Each of the 4 Dengue Serotypes for Participants in the Immunogenicity Subset

End point title	Seropositivity Rates For Each of the 4 Dengue Serotypes for Participants in the Immunogenicity Subset

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 (for each serotype). The 4 dengue virus serotypes were DENV-1, DENV-2, DENV-3 and DENV-4.PPS included all participants who received at least 1 dose of trial vaccine, who had a valid pre-dose and at least 1 valid post-dose measurement for immunogenicity and no major protocol violations. PPS included only participants from Immunogenicity Subset. 'n' indicates number analyzed are participants with data available at the given timepoint

End point type	Secondary

End point timeframe:

Months 1, 3, 6, 12, 13, 18, 24, 36, and 48

End point values	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 3 (TDV 1-Dose + Booster)	Group 4 (Placebo Control)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	83	171	174	81
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1, Day 28 (Month 1),n=83,171,174,81	97.6 (91.6 to 99.7)	97.7 (94.1 to 99.4)	100.0 (97.9 to 100.0)	49.4 (38.1 to 60.7)
DENV-2, Day 28 (Month 1),n=83,171,174,81	96.4 (89.8 to 99.2)	95.3 (91.0 to 98.0)	96.6 (92.6 to 98.7)	51.9 (40.5 to 63.1)
DENV-3, Day 28 (Month 1),n=83,171,174,81	88.0 (79.0 to 94.1)	90.1 (84.6 to 94.1)	90.8 (85.5 to 94.7)	50.6 (39.3 to 61.9)
DENV-4, Day 28 (Month 1),n=83,171,174,81	94.0 (86.5 to 98.0)	93.6 (88.8 to 96.7)	95.4 (91.1 to 98.0)	49.4 (38.1 to 60.7)
DENV-1, Day 91 (Month 3),n=83,171,174,81	95.2 (88.1 to 98.7)	97.7 (94.1 to 99.4)	99.4 (96.8 to 100.0)	51.9 (40.5 to 63.1)
DENV-2, Day 91 (Month 3),n=83,171,174,81	98.8 (93.5 to 100.0)	98.8 (95.8 to 99.9)	99.4 (96.8 to 100.0)	53.1 (41.7 to 64.3)
DENV-3, Day 91 (Month 3),n=83,171,174,81	89.2 (80.4 to 94.9)	95.3 (91.0 to 98.0)	91.4 (86.2 to 95.1)	48.1 (36.9 to 59.5)
DENV-4, Day 91 (Month 3),n=83,171,174,81	88.0 (79.0 to 94.1)	90.6 (85.3 to 94.6)	90.8 (85.5 to 94.7)	45.7 (34.6 to 57.1)
DENV-1, Day 180 (Month 6),n=83,170,174,81	100.0 (95.7 to 100.0)	97.1 (93.3 to 99.0)	99.4 (96.8 to 100.0)	49.4 (38.1 to 60.7)
DENV-2, Day 180 (Month 6),n=83,170,174,81	98.8 (93.5 to 100.0)	99.4 (96.8 to 100.0)	99.4 (96.8 to 100.0)	49.4 (38.1 to 60.7)
DENV-3, Day 180 (Month 6),n=83,170,174,81	98.8 (93.5 to 100.0)	92.9 (88.0 to 96.3)	93.1 (88.3 to 96.4)	48.1 (36.9 to 59.5)
DENV-4, Day 180 (Month 6),n=83,170,174,81	92.8 (84.9 to 97.3)	90.6 (85.2 to 94.5)	85.1 (78.9 to 90.0)	44.4 (33.4 to 55.9)
DENV-1, Day 365 (Month 12),n=79,161,164,76	98.7 (93.1 to 100.0)	97.5 (93.8 to 99.3)	97.6 (93.9 to 99.3)	57.9 (46.0 to 69.1)
DENV-2, Day 365 (Month 12),n=79,161,164,76	98.7 (93.1 to 100.0)	99.4 (96.6 to 100.0)	100.0 (97.8 to 100.0)	60.5 (48.6 to 71.6)
DENV-3, Day 365 (Month 12),n=79,161,164,76	94.9 (87.5 to 98.6)	94.4 (89.7 to 97.4)	90.2 (84.6 to 94.3)	57.9 (46.0 to 69.1)

DENV-4, Day 365 (Month 12),n=79,161,164,76	92.4 (84.2 to 97.2)	85.1 (78.6 to 90.2)	82.9 (76.3 to 88.3)	55.3 (43.4 to 66.7)
DENV-1, Day 393 (Month 13),n=80,163,167,75	97.5 (91.3 to 99.7)	95.7 (91.4 to 98.3)	100.0 (97.8 to 100.0)	60.0 (48.0 to 71.1)
DENV-2, Day 393 (Month 13),n=80,163,167,75	98.8 (93.2 to 100.0)	98.8 (95.6 to 99.9)	100.0 (97.8 to 100.0)	61.3 (49.4 to 72.4)
DENV-3, Day 393 (Month 13),n=80,163,167,75	95.0 (87.7 to 98.6)	95.1 (90.6 to 97.9)	100.0 (97.8 to 100.0)	57.3 (45.4 to 68.7)
DENV-4, Day 393 (Month 13),n=80,163,167,75	90.0 (81.2 to 95.6)	86.5 (80.3 to 91.3)	100.0 (97.8 to 100.0)	53.3 (41.4 to 64.9)
DENV-1, Day 540 (Month 18),n=81,168,172,80	95.1 (87.8 to 98.6)	97.0 (93.2 to 99.0)	98.8 (95.9 to 99.9)	62.5 (51.0 to 73.1)
DENV-2, Day 540 (Month 18),n=81,168,172,80	98.8 (93.3 to 100.0)	97.6 (94.0 to 99.3)	100.0 (97.9 to 100.0)	68.8 (57.4 to 78.7)
DENV-3, Day 540 (Month 18),n=81,168,172,80	95.1 (87.8 to 98.6)	92.3 (87.1 to 95.8)	98.3 (95.0 to 99.6)	63.8 (52.2 to 74.2)
DENV-4, Day 540 (Month 18),n=81,168,172,80	87.7 (78.5 to 93.9)	86.9 (80.8 to 91.6)	97.1 (93.3 to 99.0)	57.5 (45.9 to 68.5)
DENV-1, Day 730 (Month 24),n=71,145,148,70	100.0 (94.9 to 100.0)	95.9 (91.2 to 98.5)	100.0 (97.5 to 100.0)	68.6 (56.4 to 79.1)
DENV-2, Day 730 (Month 24),n=71,145,148,70	100.0 (94.9 to 100.0)	99.3 (96.2 to 100.0)	100.0 (97.5 to 100.0)	71.4 (59.4 to 81.6)
DENV-3, Day 730 (Month 24),n=71,145,148,70	94.4 (86.2 to 98.4)	93.1 (87.7 to 96.6)	98.6 (95.2 to 99.8)	65.7 (53.4 to 76.7)
DENV-4, Day 730 (Month 24),n=71,145,148,70	94.4 (86.2 to 98.4)	91.7 (86.0 to 95.7)	98.6 (95.2 to 99.8)	61.4 (49.0 to 72.8)
DENV-1, Day 1095 (Month 36),n=66,137,139,66	100.0 (94.6 to 100.0)	92.7 (87.0 to 96.4)	100.0 (97.4 to 100.0)	68.2 (55.6 to 79.1)
DENV-2, Day 1095 (Month 36),n=66,137,139,66	100.0 (94.6 to 100.0)	99.3 (96.0 to 100.0)	100.0 (97.4 to 100.0)	71.2 (58.7 to 81.7)
DENV-3, Day 1095 (Month 36),n=66,137,139,66	97.0 (89.5 to 99.6)	88.3 (81.7 to 93.2)	98.6 (94.9 to 99.8)	63.6 (50.9 to 75.1)
DENV-4, Day 1095 (Month 36),n=66,137,139,66	95.5 (87.3 to 99.1)	88.3 (81.7 to 93.2)	98.6 (94.9 to 99.8)	63.6 (50.9 to 75.1)
DENV-1, Day 1460 (Month 48),n=65,133,136,63	96.9 (89.3 to 99.6)	94.7 (89.5 to 97.9)	100.0 (97.3 to 100.0)	68.3 (55.3 to 79.4)
DENV-2, Day 1460 (Month 48),n=65,133,136,63	100.0 (94.5 to 100.0)	98.5 (94.7 to 99.8)	100.0 (97.3 to 100.0)	68.3 (55.3 to 79.4)
DENV-3, Day 1460 (Month 48),n=65,133,136,63	95.4 (87.1 to 99.0)	90.2 (83.9 to 94.7)	97.8 (93.7 to 99.5)	63.5 (50.4 to 75.3)
DENV-4, Day 1460 (Month 48),n=65,133,136,63	90.8 (81.0 to 96.5)	91.0 (84.8 to 95.3)	99.3 (96.0 to 100.0)	60.3 (47.2 to 72.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Solicited Local (Injection Site) Adverse Events (AEs) (Diary Recorded) by Severity in the Immunogenicity Subset of Infant/Toddler Following each Vaccination

End point title	Percentage of Participants with Solicited Local (Injection Site) Adverse Events (AEs) (Diary Recorded) by Severity in the Immunogenicity Subset of Infant/Toddler Following each Vaccination

End point description:

Solicited local injection included pain, erythema at injection site, and swelling at injection site. They were collected using a diary and graded as [Grade 0 (no pain), 1 (mild: minor reaction to touch), 2 (moderate: cries/protests on touch) and 3 (severe: cries when limb is moved/spontaneously painful)].

Erythema and Swelling at injection site were graded as Grade 0 (<10 mm), 1 (mild: ≥10 – ≤ 20 mm), 2 (moderate: > 20 – ≤ 40 mm) and 3 (severe: > 40 mm).Safety Analysis Set included all participants who received at least 1 dose of trial vaccine. Only participants in immunogenicity subset were included. Data were summarized separately for each age group. 'n' indicates number analyzed are participants with data available for the category. Only categories for which there was at least 1 participant are reported.

End point type	Secondary

End point timeframe:

Within 7 days after each vaccination

End point values	Group 1 (TDV 2-Dose) Infant/Toddler	Group 2 (TDV 1-Dose) Infant/Toddler	Group 3 (TDV 2-Dose) Infant/Toddler	Group 4 (Placebo Control) Infant/Toddler
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	60	62	32
Units: percentage of participants				
number (not applicable)				
After Vaccination 1, Pain: Any, n=27,54,55,28	11.1	5.6	12.7	7.1
After Vaccination 1, Pain: Mild,n=27,54,55,28	11.1	1.9	10.9	3.6
After Vaccination 1, Pain: Moderate, n=27,54,55,28	0	3.7	1.8	3.6
After Vaccination 1, Erythema: Any, n=27,53,55,27	0	3.8	3.6	0
After Vaccination1,Erythema (1-2 cm),n=27,53,55,27	0	3.8	3.6	0
After Vaccination 1, Swelling: Any, n=27,53,55,27	0	3.8	0	0
After Vaccination 1,Swelling(1-2 cm),n=27,53,55,27	0	3.8	0	0
After Vaccination 2,Pain: Any,n=26,53,54,29	3.8	3.8	13.0	6.9
After Vaccination 2, Pain: Mild, n=26,53,54,29	3.8	3.8	9.3	6.9
After Vaccination 2, Pain: Moderate, n=26,53,54,29	0	0	3.7	0
After Vaccination 3, Pain: Any, n=27,56,60,29	7.4	8.9	15.0	3.4
After Vaccination 3, Pain: Mild, n=27,56,60,29	7.4	7.1	11.7	3.4
After Vaccination 3, Pain: Moderate, n=27,56,60,29	0	1.8	1.7	0
After Vaccination 3, Pain: Severe, n=27,56,60,29	0	0	1.7	0
After Vaccination 3, Swelling: Any, n=27,56,59,29	0	0	1.7	0
After Vaccination3,Swelling(1-2 cm),n=27,56,59,29	0	0	1.7	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Solicited Local (Injection Site) Adverse Events (AEs) (Diary Recorded) by Severity in the Immunogenicity Subset of Adult/Children Following each Vaccination

End point title	Percentage of Participants with Solicited Local (Injection Site) Adverse Events (AEs) (Diary Recorded) by Severity in the Immunogenicity Subset of Adult/Children Following each Vaccination

End point description:

Solicited local injection site reactions were collected by participant diary and graded as [Grade 0 (no pain), 1 (mild: no interference with daily activity), 2 (moderate: interference with daily activity with or without treatment) and 3 (severe: prevents daily activity with or without treatment)]. Erythema and Swelling at injection site were graded as Grade 0 (<25 mm), 1 (mild: ≥25 – ≤ 50 mm), 2 (moderate: > 50 – ≤ 100 mm).Safety Analysis Set included all participants who received at least 1 dose of trial vaccine. Only participants in immunogenicity subset were included. Data were summarized separately for each age group. 'n' indicates number analyzed are participants with data available for the category. Only categories for which there was at least 1 participant are reported

End point type	Secondary

End point timeframe:

Within 7 days after each vaccination

End point values	Group 1 (TDV 2-Dose) Adult/Children	Group 2 (TDV 1-Dose) Adult/Children	Group 3 (TDV 1-Dose + Booster) Adult/Children	Group 4 (Placebo Control) Adult/Children
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	62	127	129	61
Units: percentage of participants				
number (not applicable)				
After Vaccination 1, Pain:Any, n=60,126,123,57	25.0	31.7	26.8	8.8
After Vaccination 1, Pain:Mild, n=60,126,123,57	23.3	28.6	22.0	7.0
After Vaccination 1, Pain:Moderate,n=60,126,123,57	1.7	2.4	4.1	1.8
After Vaccination 1, Pain:Severe,n=62,126,123,57	0	0.8	0.8	0
After Vaccination 1, Erythema:Any,n=60,126,122,57	0	0.8	0	0
AfterVaccination1Erythema(2.5-5 cm)n=60,126,122,57	0	0.8	0	0
After Vaccination 1, Swelling:Any,n=60,126,122,57	0	0	0	1.8
AfterVaccination1Swelling(2.5-5 cm)n=60,126,122,57	0	0	0	1.8
After Vaccination 2, Pain:Any, n=60,116,119,55	31.7	18.1	10.9	14.5
After Vaccination 2, Pain:Mild, n=60,116,119,55	20.0	16.4	6.7	10.9
After Vaccination 2,Pain: Moderate,n=60,116,119,55	5.0	0	4.2	1.8
After Vaccination 2, Pain:Severe, n=60,116,119,55	6.7	1.7	0	1.8
After Vaccination 3, Pain:Any, n=59,115,120,55	16.9	20.0	19.2	16.4

After Vaccination 3, Pain: Mild,n=59,115,120,55	13.6	18.3	15.8	12.7
After Vaccination 3, Pain:Moderate,n=59,115,120,55	3.4	0	3.3	3.6
After Vaccination 3, Pain:Severe, n=59,115,120,55	0	1.7	0	0
AfterVaccination3, Erythema:Any,n=58,115,120,55	0	0	0.8	0
AfterVaccination3,Erythema,2.5-5cm,n=58,115,120,55	0	0	0.8	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Solicited Systemic Adverse Events (AEs) (Diary Recorded) by Severity in the Immunogenicity Subset of Infant/Toddler Following each Vaccination

End point title	Percentage of Participants with Solicited Systemic Adverse Events (AEs) (Diary Recorded) by Severity in the Immunogenicity Subset of Infant/Toddler Following each Vaccination

End point description:

Solicited systemic AEs included drowsiness, graded as 0-behavior as usual, 1-mild: drowsiness easily tolerated, 2-moderate: drowsiness that interferes with normal activity and 3-severe: prevents normal activity with/without treatment; irritability/fussiness, graded as 0-behavior as usual, mild: crying more than usual/no effect on normal activity, moderate: crying more than usual/interferes with normal activity and severe: crying that cannot be comforted/prevents normal; loss of appetite, graded as 0-apetite as usual, mild: eating less than usual/no effect on normal activity, moderate: eating less than usual/interferes with normal activity, severe: not eating at all. A systemic AE of fever (≥38°C or ≥100.4°F) was recorded but excluded from overall count as no severity grading was applied for it. Safety Analysis Set from immunogenicity subset. Data were summarized for each age group. 'n'=participants with data available for the category. Only categories with data are reported.

End point type	Secondary

End point timeframe:

Within 14 days after each vaccination

End point values	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 3 (TDV 1-Dose + Booster)	Group 4 (Placebo Control)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	60	62	32
Units: percentage of participants				
number (not applicable)				
After Vaccination 1,Irritability:Any,n=27,54,55,28	3.7	1.9	9.1	0
After Vac.1,Irritability:Mild,n=27,54,55,28	3.7	0	3.6	0
After Vac.1,Irritability:Moderate ,n=27,54,55,27	0	1.9	3.6	0
After Vac. 1, Irritability: Severe, n=27,54,55,27	0	0	1.8	0
After Vac. 1,Drowsiness: Any, n=27,54,55,28	0	7.4	7.3	7.1

After Vac.1, Drowsiness: Mild, n=27,54,55,28	0	7.4	5.5	7.1
After Vac.1, Drowsiness: Moderate, n=27,54,55,28	0	0	1.8	0
After Vac.1,Loss of Appetite:Any, n=27,54,55,28	7.4	9.3	10.9	7.1
After Vac.1,Loss of Appetite:Mild, n=27,54,55,28	7.4	7.4	5.5	0
After Vac.1Loss of Appetite:Moderate,n=27,54,55,28	0	1.9	3.6	7.1
After Vac.1,Loss of Appetite:Severe, n=27,54,55,28	0	0	1.8	0
After Vac.1Fever Any, n=25,50,52,27	0	6.0	5.8	3.7
After Vac.1,Fever (38.0 - < 38.5 °C),n=25,50,52,27	0	2.0	3.8	0
After Vac.1,Fever (38.5 - < 39.0 °C),n=25,50,52,27	0	4.0	1.9	3.7
After Vac.2,Irritability: Any, n=26,53,53,28	15.4	1.9	1.9	10.7
After Vac.2, Irritability: Mild, n=26,53,53,28	15.4	1.9	1.9	10.7
After Vac.2, Drowsiness: Any, n=26,53,53,28	3.8	3.8	3.8	0
After Vac.2, Drowsiness: Mild,n=26,53,53,28	3.8	3.8	3.8	0
After Vac.2, Loss of Appetite: Any, n=26,53,53,28	7.7	13.2	5.7	0
After Vac.2, Loss of Appetite: Mild,n=26,53,53,28	3.8	9.4	5.7	0
After Vac.2Loss of Appetite:Moderate,n=26,53,53,28	3.8	1.9	0	0
After Vac.2,Loss of Appetite:Severe, n=26,53,53,28	0	1.9	0	0
After Vac.2,Fever,Any, n=25,52,52,28	16.0	9.6	11.5	3.6
After Vac.2,Fever (38.0 - < 38.5 °C),n=25,52,52,28	0	3.8	5.8	0
After Vac.2,Fever (38.5 - < 39.0 °C),n=25,52,52,28	8.0	5.8	3.8	3.6
After Vac.2,Fever (39.0 - < 39.5 °C),n=25,52,52,28	4.0	0	1.9	0
After Vac.2,Fever (39.5 - < 40.0 °C),n=25,52,52,28	4.0	0	0	0
After Vac.3,Irritability: Any, n=27,56,59,29	3.7	0	1.7	10.3
After Vac.3, Irritability: Mild, n=27,56,59,29	3.7	0	0	6.9
After Vac.3, Irritability: Moderate,n=27,56,59,29	0	0	1.7	3.4
After Vac.3,Drowsiness: Any, n=27,56,59,29	3.7	3.6	3.4	3.4
After Vac.1,Drowsiness: Mild,n=27,56,59,29	3.7	3.6	1.7	0
After Vac.1,Drowsiness: Moderate,n=27,56,59,29	0	0	1.7	0
After Vac.3,Drowsiness: Severe,n=27,56,59,29	0	0	0	3.4
After Vac.3,Loss of Appetite: Any,n=27,56,59,29	7.4	12.5	3.4	10.3
After Vac.3, Loss of Appetite: Mild,n=27,56,59,29	3.7	7.1	3.4	6.9
After Vac.3,Lossof Appetite:Moderate,n=27,56,59,29	3.7	5.4	0	3.4

After Vac.3 Fever:Any, n=26,55,60,29	0	3.6	3.3	6.9
After Vac.3,Fever(38.0 - < 38.5 °C), n=26,55,60,29	0	0	1.7	3.4
After Vac.3,Fever (38.5 - < 39.0 °C) n=26,55,60,29	0	1.8	1.7	0
After Vac.3,Fever (39.0 - < 39.5 °C) n=26,55,60,29	0	1.8	0	3.4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Solicited Systemic Adverse Events (AEs) (Diary Recorded) by Severity in the Immunogenicity Subset of Adult/Children Following each Vaccination

End point title	Percentage of Participants with Solicited Systemic Adverse Events (AEs) (Diary Recorded) by Severity in the Immunogenicity Subset of Adult/Children Following each Vaccination

End point description:

Solicited systemic AEs were collected after vaccination and included headache, asthenia, malaise, myalgia and fever. Severity scales for headache were none, mild: no interference with daily activity, moderate: interference with daily activity with or without treatment and severe: prevents normal activity with or without treatment. Severity scales for others were none, mild: no interference with daily activity, moderate: interference with daily activity and severe: prevents daily activity. A systemic AE of fever (defined as ≥38°C or ≥100.4°F) was recorded but excluded from the overall count as no severity grading was applied for it. Safety Analysis Set from immunogenicity subset. Data were summarized for each age group. 'n'=participants with data available for the category. Only categories with data are reported.

End point type	Secondary

End point timeframe:

Within 14 days after each vaccination

End point values	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 3 (TDV 1-Dose + Booster)	Group 4 (Placebo Control)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	127	129	61
Units: percentage of participants				
number (not applicable)				
After Vac.1, Headache: Any, n=60,126,123,57	20.0	23.8	16.3	21.1
After Vac.1, Headache: Mild, n=60,126,123,57	16.7	20.6	13.0	14.0
After Vac.1, Headache:Moderate, n=60,126,123,57	3.3	2.4	1.6	5.3
After Vac.1, Headache: Severe, n=60,126,123,57	0	0.8	1.6	1.8
After Vac.1, Asthenia: Any, n=60,126,123,57	5.0	11.1	7.3	7.0
After Vac.1, Asthenia: Mild, n=60,126,123,57	3.3	10.3	4.9	3.5
After Vac.1, Asthenia: Moderate,n=60,126,123,57	1.7	0.8	1.6	3.5

After Vac.1, Asthenia: Severe,n=60,126,123,57	0	0	0.8	0
After Vac.1, Malaise: Any, n=60,126,123,57	8.3	14.3	8.9	10.5
After Vac.1, Malaise: Mild, n=60,126,123,57	6.7	13.5	7.3	8.8
After Vac.1, Malaise: Moderate,n=60,126,123,57	1.7	0.8	0.8	0
After Vac.1, Malaise: Severe, n=60,126,123,57	0	0	0.8	1.8
After Vac.1, Myalgia: Any, n=60,126,123,57	10.0	20.6	11.4	7.0
After Vac.1, Myalgia: Mild, n=60,126,123,57	8.3	18.3	10.6	7.0
After Vac.1, Myalgia: Moderate,n=60,126,123,57	1.7	2.4	0	0
After Vac.1, Myalgia: Severe, n=60,126,123,57	0	0	0.8	0
After Vac.1, Fever: Any, n=51,119,110,51	5.9	2.5	4.5	5.9
After Vac.1,Fever:38.0 - < 38.5 °C,n=51,119,110,51	2.0	1.7	0	2.0
After Vac.1,Fever:38.5 - < 39.0 °C,n=51,119,110,51	2.0	0	1.8	3.9
After Vac.1,Fever:39.0-< 39.5°C,n=51,119,110,51	2.0	0.8	0.9	0
After Vac.1,Fever: 39.5-< 40.0 °C,n=51,119,110,51	0	0	1.8	0
After Vac.2,Headache:Any,n=59,115,118,55	18.6	9.6	6.8	16.4
After Vac.2,Headache:Mild,n=59,115,118,55	11.9	7.8	4.2	12.7
After Vac.2,Headache:Moderate,n=59,115,11	5.1	0.9	2.5	1.8
After Vac.2,Headache:Severe,n=59,115,118,	1.7	0.9	0	1.8
After Vac.2,Asthenia:Any,n=59,115,118,55	8.5	7.8	4.2	3.6
After Vac.2,Asthenia:Mild,n=59,115,118,55	5.1	7.0	2.5	3.6
After Vac.2,Asthenia:Moderate,n=59,115,118	1.7	0	1.7	0
After Vac.2,Asthenia:Severe,n=59,115,118,5	1.7	0.9	0	0
After Vac.2,Malaise:Any,n=59,115,118,55	15.3	8.7	6.8	9.1
After Vac.2, Malaise: Mild, n=59,115,118,55	10.2	6.1	4.2	7.3
After Vac.2, Malaise: Moderate,n=59,115,118,55	3.4	1.7	1.7	0
After Vac.2, Malaise: Severe,n=59,115,118,55	1.7	0.9	0.8	1.8
After Vac.2, Myalgia: Any, n=59,115,118,55	16.9	5.2	5.9	5.5
After Vac.2, Myalgia: Mild, n=59,115,118,55	10.2	5.2	2.5	5.5
After Vac.2, Myalgia: Moderate,n=59,115,118,55	3.4	0	2.5	0
After Vac.2, Myalgia: Severe,n=59,115,118,55	3.4	0	0.8	0
After Vac.2, Fever: Any, n=51,104,110,49	2.0	2.9	2.7	4.1

After Vac.2,Fever:38.0-< 38.5 °C,n=51,104,110,49	2.0	1.0	0.9	0
After Vac.2,Fever:38.5-< 39.0°C,n=51,104,110,49	0	1.0	0.9	2.0
AfterVac.2,Fever: 39.5-<40.0 °C,n=51,104,110,49	0	1.0	0.9	2.0
After Vac.3, Headache: Any, n=59,115,120,55	10.2	11.3	7.5	7.3
After Vac.3, Headache: Mild, n=59,115,120,55	10.2	7.8	5.8	5.5
After Vac.3, Headache: Moderate,n=59,115,120,55	0	1.7	1.7	0
After Vac.3, Headache: Severe,n=59,115,120,55	0	1.7	0	1.8
After Vac.3, Asthenia: Any, n=59,115,120,55	6.8	7.0	2.5	7.3
After Vac.3, Asthenia: Mild, n=59,115,120,55	6.8	5.2	2.5	7.3
After Vac.3, Asthenia: Moderate,n=59,115,120,55	0	0.9	0	0
After Vac.3, Asthenia: Severe,n=59,115,120,55	0	0.9	0	0
After Vac.3,Malaise: Any, n=59,115,120,55	5.1	7.8	8.3	3.6
After Vac.3,Malaise: Mild, n=59,115,120,55	3.4	5.2	5.8	1.8
After Vac.3,Malaise: Moderate,n=59,115,120,55	0	0.9	1.7	1.8
After Vac.3,Malaise: Severe,n=59,115,120,55	1.7	1.7	0.8	0
After Vac.3,Myalgia: Any, n=59,115,120,55	6.8	11.3	8.3	5.5
After Vac.3,Myalgia: Mild, n=59,115,120,55	5.1	9.6	5.8	5.5
After Vac.3,Myalgia: Moderate,n=59,115,120,55	0	0.9	1.7	0
After Vac.3,Myalgia:Severe,n=59,115,120,55	1.7	0.9	0.8	0
After Vac.3,Fever:Any,n=56,106,115,51	1.8	1.9	1.7	2.0
After Vac.3,Fever:38.0 - < 38.5 °C,n=56,106,115,51	0	1.9	0.9	2.0
After Vac.3,Fever:38.5 - < 39.0 °C,n=56,106,115,51	0	0	0.9	0
After Vac.3,Fever:39.0 - < 39.5 °C,n=56,106,115,51	1.8	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Any Unsolicited Adverse Events (AEs) in the Immunogenicity Subset Following each Vaccination

End point title	Percentage of Participants with Any Unsolicited Adverse Events (AEs) in the Immunogenicity Subset 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 Analysis Set included all participants who received at least 1 dose of trial vaccine. Only participants in the

immunogenicity subset were included. 'n' indicates number analyzed is number of participants with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Within 28 days after each vaccination

End point values	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 3 (TDV 1-Dose + Booster)	Group 4 (Placebo Control)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	91	187	191	93
Units: percentage of participants				
number (not applicable)				
After Vaccination 1,n=91,187,191,93	19.8	20.3	19.4	21.5
After Vaccination 2,n=90,176,181,87	12.2	10.2	11.0	16.1
After Vaccination 3,n=88,172,179,84	6.8	12.8	10.1	9.5

Statistical analyses

No statistical analyses for this end point

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

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

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 Analysis Set included all participants who received at least 1 dose of trial vaccine.

End point type	Secondary

End point timeframe:

From first vaccination through end of study (Day 1460)

End point values	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 3 (TDV 1-Dose + Booster)	Group 4 (Placebo Control)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200	398	998	198
Units: percentage of participants				
number (not applicable)	5.0	4.5	6.5	5.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Febrile Episodes of Virologically Confirmed Dengue with Onset 30 days Post-first Vaccination

End point title	Percentage of Participants with Febrile Episodes of Virologically Confirmed Dengue with Onset 30 days Post-first Vaccination

End point description:

Participants with febrile illness (defined as temperature ≥ 38°C on 2 consecutive days) were evaluated for dengue. A dengue infection was considered virologically confirmed by either positive polymerase chain reaction (PCR) or NS1 enzyme-linked immunosorbent assay (ELISA). virologically confirmed dengue with onset 30 days after first vaccination within each group.Safety Analysis Set included all participants who received at least 1 dose of trial vaccine.

End point type	Secondary

End point timeframe:

From 30 days post-first vaccination through end of study (Day 1460)

End point values	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 3 (TDV 1-Dose + Booster)	Group 4 (Placebo Control)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200	398	998	198
Units: percentage of participants				
number (not applicable)	3.5	2.0	2.2	6.6

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality and Serious adverse events: From first vaccination (Day 1) through end of study (Day 540); Other adverse events: From any vaccination (Day 1, Day 91, and Day 365) up to 28 days post vaccination.

Adverse event reporting additional description:

Safety Analysis Set included all participants who received at least 1 dose of trial vaccine. Data for other (non-serious) adverse events is reported for participants from Immunogenicity Subset with available data for analyses.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Group 1 (TDV 2-Dose)

Reporting group description:

Takeda's tetravalent dengue vaccine candidate (TDV), 0.5 mL, subcutaneous injection on Days 1 and 91. Placebo-matching, 0.5 mL, subcutaneous injection on Day 365.

Reporting group title	Group 2 (TDV 1-Dose)

Reporting group description:

Takeda's TDV, 0.5 mL, subcutaneous injection on Day 1. Placebo-matching, 0.5 mL, subcutaneous injection on Days 91 and 365.

Reporting group title	Group 4 (Placebo Control)

Reporting group description:

Placebo matching, 0.5 mL, subcutaneous injection on Days 1, 91 and 365.

Reporting group title	Group 3 (TDV 1-Dose + Booster)

Reporting group description:

Takeda's TDV, 0.5 mL, subcutaneous injection on Days 1 and 365. Placebo-matching, 0.5 mL, subcutaneous injection on Day 91.

Serious adverse events	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 4 (Placebo Control)
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 200 (5.00%)	18 / 398 (4.52%)	10 / 198 (5.05%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Teratoma Benign			
subjects affected / exposed	1 / 200 (0.50%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Finger Amputation			

subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature Baby			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Dehiscence			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Food Allergy			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Homicide			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian Cyst			

subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian Cyst Torsion			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthmatic Crisis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	1 / 200 (0.50%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple Injuries			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal Injury			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle Fracture			
subjects affected / exposed	1 / 200 (0.50%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropod Bite			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropod Sting			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burns Second Degree			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial Bones Fracture			
subjects affected / exposed	1 / 200 (0.50%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised Tonic-Clonic			

subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Relapsing-Remitting Multiple Sclerosis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Immune Thrombocytopenic Purpura			
subjects affected / exposed	1 / 200 (0.50%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Ocular Myasthenia			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus Paralytic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal Hernia			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Obstruction			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Glomerulonephritis Acute			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephritic Syndrome			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Aneurysmal Bone Cyst			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Amoebic Dysentery			
subjects affected / exposed	1 / 200 (0.50%)	1 / 398 (0.25%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 200 (0.00%)	2 / 398 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	2 / 200 (1.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess Limb			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascariasis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dengue Fever			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scarlet Fever			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amoebiasis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis Perforated			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burkholderia Cepacia Complex Sepsis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalomyelitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Rotavirus			

subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious Colitis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal Abscess			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar Abscess			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Tuberculosis			

subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			
subjects affected / exposed	0 / 200 (0.00%)	1 / 398 (0.25%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sinusitis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth Abscess			
subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			

subjects affected / exposed	0 / 200 (0.00%)	0 / 398 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 200 (0.50%)	0 / 398 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 3 (TDV 1-Dose + Booster)		
Total subjects affected by serious adverse events			
subjects affected / exposed	65 / 998 (6.51%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Teratoma Benign			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Finger Amputation			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Premature Baby			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Dehiscence			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Food Allergy			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Homicide			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian Cyst Torsion			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthmatic Crisis			
subjects affected / exposed	4 / 998 (0.40%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Asthma			

subjects affected / exposed	2 / 998 (0.20%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchospasm				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Contusion				
subjects affected / exposed	2 / 998 (0.20%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Head Injury				
subjects affected / exposed	2 / 998 (0.20%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Multiple Injuries				
subjects affected / exposed	3 / 998 (0.30%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Abdominal Injury				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ankle Fracture				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthropod Bite				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthropod Sting				

subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Burns Second Degree				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial Bones Fracture				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Seizure				
subjects affected / exposed	2 / 998 (0.20%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised Tonic-Clonic				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Migraine				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Relapsing-Remitting Multiple Sclerosis				

subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Immune Thrombocytopenic Purpura			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Ocular Myasthenia			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 998 (0.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus Paralytic			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Inguinal Hernia				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal Obstruction				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Volvulus				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Glomerulonephritis Acute				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nephritic Syndrome				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Aneurysmal Bone Cyst				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Amoebic Dysentery				
subjects affected / exposed	5 / 998 (0.50%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				

subjects affected / exposed	5 / 998 (0.50%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	4 / 998 (0.40%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	5 / 998 (0.50%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Urinary Tract Infection				
subjects affected / exposed	4 / 998 (0.40%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Abscess Limb				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ascariasis				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dengue Fever				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Scarlet Fever				
subjects affected / exposed	2 / 998 (0.20%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Amoebiasis				

subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis Perforated			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Burkholderia Cepacia Complex Sepsis			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalomyelitis			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endometritis			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis Rotavirus			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis A			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infectious Colitis			

subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nasal Abscess				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonsillar Abscess				
subjects affected / exposed	1 / 998 (0.10%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngotonsillitis				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary Tuberculosis				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 998 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Tract Infection				

subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic Shock			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tooth Abscess			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral Infection			
subjects affected / exposed	0 / 998 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 998 (0.10%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1 (TDV 2-Dose)	Group 2 (TDV 1-Dose)	Group 4 (Placebo Control)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 200 (8.50%)	43 / 398 (10.80%)	22 / 198 (11.11%)
Nervous system disorders			
Headache			
subjects affected / exposed[1]	1 / 91 (1.10%)	2 / 187 (1.07%)	1 / 93 (1.08%)
occurrences (all)	1	2	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed[2]	2 / 91 (2.20%)	1 / 187 (0.53%)	1 / 93 (1.08%)
occurrences (all)	2	1	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed[3]	0 / 91 (0.00%)	0 / 187 (0.00%)	2 / 93 (2.15%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed[4]	1 / 91 (1.10%)	4 / 187 (2.14%)	2 / 93 (2.15%)
occurrences (all)	1	4	2
Vomiting			
subjects affected / exposed[5]	1 / 91 (1.10%)	3 / 187 (1.60%)	3 / 93 (3.23%)
occurrences (all)	1	3	3
Respiratory, thoracic and mediastinal disorders			
Nasal Congestion			
subjects affected / exposed[6]	0 / 91 (0.00%)	1 / 187 (0.53%)	2 / 93 (2.15%)
occurrences (all)	0	2	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed[7]	10 / 91 (10.99%)	25 / 187 (13.37%)	10 / 93 (10.75%)
occurrences (all)	11	31	10
Viral Infection			
subjects affected / exposed[8]	1 / 91 (1.10%)	4 / 187 (2.14%)	2 / 93 (2.15%)
occurrences (all)	1	4	2
Bronchitis			

subjects affected / exposed[9]	0 / 91 (0.00%)	4 / 187 (2.14%)	0 / 93 (0.00%)
occurrences (all)	0	5	0
Tonsillitis			
subjects affected / exposed[10]	2 / 91 (2.20%)	3 / 187 (1.60%)	0 / 93 (0.00%)
occurrences (all)	2	3	0
Parasitic Gastroenteritis			
subjects affected / exposed[11]	2 / 91 (2.20%)	0 / 187 (0.00%)	2 / 93 (2.15%)
occurrences (all)	2	0	2
Gastroenteritis			
subjects affected / exposed[12]	1 / 91 (1.10%)	7 / 187 (3.74%)	5 / 93 (5.38%)
occurrences (all)	1	7	6

Non-serious adverse events	Group 3 (TDV 1-Dose + Booster)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 998 (4.11%)		
Nervous system disorders			
Headache			
subjects affected / exposed[1]	5 / 191 (2.62%)		
occurrences (all)	5		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed[2]	2 / 191 (1.05%)		
occurrences (all)	2		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed[3]	2 / 191 (1.05%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed[4]	2 / 191 (1.05%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed[5]	0 / 191 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			

Nasal Congestion subjects affected / exposed[6] occurrences (all)	0 / 191 (0.00%) 0		
Infections and infestations Nasopharyngitis subjects affected / exposed[7] occurrences (all)	21 / 191 (10.99%) 22		
Viral Infection subjects affected / exposed[8] occurrences (all)	4 / 191 (2.09%) 4		
Bronchitis subjects affected / exposed[9] occurrences (all)	3 / 191 (1.57%) 3		
Tonsillitis subjects affected / exposed[10] occurrences (all)	2 / 191 (1.05%) 2		
Parasitic Gastroenteritis subjects affected / exposed[11] occurrences (all)	1 / 191 (0.52%) 1		
Gastroenteritis subjects affected / exposed[12] occurrences (all)	5 / 191 (2.62%) 6		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Non-serious adverse events were based on Immunogenicity Set.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 July 2015	Study duration was extended from 18 months to 48 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported