Clinical trial results:
A Phase 3, Follow-Up Trial to Evaluate Long-Term Safety and Antibody Persistence, and the Impact of a Booster Dose of a Tetravalent Dengue Vaccine Candidate in Healthy Adolescents and Adults in Areas Non-Endemic for Dengue

Summary

EudraCT number	2023-000027-36
Trial protocol	Outside EU/EEA
Global end of trial date	25 May 2024

Results information

Result version number	v2 (current)
This version publication date	18 July 2026
First version publication date	08 June 2025
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	DEN-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03999996
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Ave, Lexington, MA, United States, 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to evaluate the long-term safety and antibody persistence, and the impact of a booster dose of TDV.

Protection of trial subjects:

Each participant or their parents/guardians/legally authorized representatives signed an informed consent form (ICF) before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2019
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	United States: 246
Country: Number of subjects enrolled	Mexico: 119
Worldwide total number of subjects	365
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)	79
Adults (18-64 years)	286
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at multiple investigative sites in United States (US) and Mexico from 12 November 2019 to 25 May 2024.

Pre-assignment

Screening details:

Healthy participants who received Takeda's Dengue Tetravalent Vaccine (TDV) in two parent trials, DEN-304 [NCT03423173] and DEN-315 [NCT03341637] were enrolled to receive either placebo or TDV.

Period 1

Period 1 title	Prior to Booster
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Prior to Booster: DEN-304

Arm description:

Participants who received TDV in parent trial DEN-304 (US) were assessed before they received booster dose (Placebo/TDV) at Visit 3 (Month 15).

Arm type	Experimental
Investigational medicinal product name	TDV
Investigational medicinal product code	
Other name	Takeda’s Dengue Tetravalent Vaccine (TDV)
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Month 15

Arm title	Prior to Booster: DEN-315

Arm description:

Participants who received TDV in parent trial DEN-315 (Mexico) were assessed before they received booster dose (Placebo/TDV) at Visit 3 (Month 42).

Arm type	Experimental
Investigational medicinal product name	TDV
Investigational medicinal product code	
Other name	Takeda’s Dengue Tetravalent Vaccine (TDV)
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Month 42

Number of subjects in period 1	Prior to Booster: DEN-304	Prior to Booster: DEN-315
Started	246	119
Completed	149	84
Not completed	97	35
Withdrawal of Consent	51	8
Adverse event, serious fatal	-	1
Adverse event, non-fatal	2	-
Reason Not Specified	27	4
Lost to follow-up	17	22

Period 2

Period 2 title	Booster Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Data analyst, Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Booster Phase: Placebo

Arm description:

Participants received TDV placebo-matching 0.5 ml injection, SC, once at Visit 3 (Month 15) for participants from parent trial DEN-304 (US) or once at Visit 3 (Month 42) for participants from parent trial DEN-315 (Mexico).

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

Dosage and administration details:

0.5 ml injection, SC, once at Month 15 for participants from parent trial DEN-304 (US) or once at Month 42 for participants from parent trial DEN-315 (Mexico).

Arm title	Booster Phase: TDV

Arm description:

Participants received TDV 0.5 ml, injection, SC, once at Visit 3 (Month 15) for participants from parent trial DEN-304 (US) or once at Visit 3 (Month 42) for participants from parent trial DEN-315 (Mexico).

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

Dosage and administration details:

0.5 ml injection, SC, once at Month 15 for participants from parent trial DEN-304 (US) or once at Month

42 for participants from parent trial DEN-315 (Mexico).

Number of subjects in period 2	Booster Phase: Placebo	Booster Phase: TDV
Started	118	115
Completed	115	110
Not completed	3	5
Withdrawal of Consent	-	1
Reason Not Specified	-	1
Lost to follow-up	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Prior to Booster: DEN-304
Reporting group description:	
Participants who received TDV in parent trial DEN-304 (US) were assessed before they received booster dose (Placebo/TDV) at Visit 3 (Month 15).	
Reporting group title	Prior to Booster: DEN-315
Reporting group description:	
Participants who received TDV in parent trial DEN-315 (Mexico) were assessed before they received booster dose (Placebo/TDV) at Visit 3 (Month 42).	

Reporting group values	Prior to Booster: DEN-304	Prior to Booster: DEN-315	Total
Number of subjects	246	119	365
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	44.4	16.3	
standard deviation	± 11.03	± 1.77	-
Gender categorical Units: Subjects			
Female	145	70	215
Male	101	49	150
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	2	3
Asian	4	0	4
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	35	0	35
White	201	0	201
More than one race	4	117	121
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	119	127
Not Hispanic or Latino	238	0	238
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Prior to Booster: DEN-304
Reporting group description:	
Participants who received TDV in parent trial DEN-304 (US) were assessed before they received booster dose (Placebo/TDV) at Visit 3 (Month 15).	
Reporting group title	Prior to Booster: DEN-315
Reporting group description:	
Participants who received TDV in parent trial DEN-315 (Mexico) were assessed before they received booster dose (Placebo/TDV) at Visit 3 (Month 42).	
Reporting group title	Booster Phase: Placebo
Reporting group description:	
Participants received TDV placebo-matching 0.5 ml injection, SC, once at Visit 3 (Month 15) for participants from parent trial DEN-304 (US) or once at Visit 3 (Month 42) for participants from parent trial DEN-315 (Mexico).	
Reporting group title	Booster Phase: TDV
Reporting group description:	
Participants received TDV 0.5 ml, injection, SC, once at Visit 3 (Month 15) for participants from parent trial DEN-304 (US) or once at Visit 3 (Month 42) for participants from parent trial DEN-315 (Mexico).	

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 1 (Month 0 [Day 1])

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 1 (Month 0 [Day 1])[1]
End point description:	
GMTs of neutralizing antibodies were measured by microneutralization test 50% (MNT50) for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 1 at Month 0 for participants from both parent trials (DEN-304 and DEN-315). Per Protocol Set (PPS) included all participants from the Full Analysis Set (FAS) who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial.	
End point type	Primary
End point timeframe:	
Month 0 (Day 1)	
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: Only descriptive analyses were planned for this endpoint.	

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	119		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	76.8 (62.0 to 95.2)	88.6 (70.4 to 111.5)		
DENV-2	539.6 (460.9 to 631.7)	425.6 (352.7 to 513.5)		

DENV-3	33.7 (28.0 to 40.5)	29.5 (24.1 to 36.1)		
DENV-4	40.0 (33.1 to 48.4)	27.1 (21.9 to 33.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 2 (Month 12)

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 2 (Month 12)[2]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 2 at Month 12 for participants from both parent trials (DEN-304 and DEN-315). PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 12

Notes:

[2] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	48		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	58.4 (45.0 to 75.7)	96.4 (69.9 to 132.7)		
DENV-2	427.3 (360.2 to 507.0)	276.1 (208.3 to 365.9)		
DENV-3	32.8 (26.5 to 40.4)	25.3 (18.5 to 34.7)		
DENV-4	30.1 (24.5 to 37.1)	22.9 (17.6 to 29.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 15) (DEN-304)

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 15) (DEN-304)[3][4]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 3 at Month 15 for participants from parent trial DEN-304. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 15 (DEN-304)

Notes:

[3] - 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: Only descriptive analyses were planned for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-304 was included for this endpoint.

End point values	Prior to Booster: DEN-304			
Subject group type	Reporting group			
Number of subjects analysed	171			
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	121.7 (93.3 to 158.7)			
DENV-2	560.2 (473.9 to 662.2)			
DENV-3	40.3 (32.6 to 49.8)			
DENV-4	37.6 (29.9 to 47.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 42) (DEN-315)

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 42) (DEN-315)[5][6]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 3 at Month 42 for participants from parent trial DEN-315. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 42 (DEN-315)

Notes:

[5] - 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: Only descriptive analyses were planned for this endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-315 was included for this endpoint.

End point values	Prior to Booster: DEN-315			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	106.5 (80.8 to 140.4)			
DENV-2	202.9 (159.5 to 258.2)			
DENV-3	21.9 (16.8 to 28.5)			
DENV-4	15.8 (12.2 to 20.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 1 (Month 0 [Day 1])

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 1 (Month 0 [Day 1])[7]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 1 at Month 0 for participants from both parent trials (DEN-304 and DEN-315). PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Month 0 [Day 1)

Notes:

[7] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	119		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial BL Serostatus:Positive: DENV-1	122.8 (59.5 to 253.2)	259.3 (135.7 to 495.5)		
Parent Trial BL Serostatus:Positive: DENV-2	560.1 (314.3 to 998.1)	714.1 (355.2 to 1435.7)		
Parent Trial BL Serostatus:Positive: DENV-3	48.2 (26.1 to 88.9)	118.7 (28.3 to 497.3)		
Parent Trial BL Serostatus:Positive: DENV-4	61.5 (32.1 to 118.2)	112.4 (29.6 to 427.5)		
Parent Trial BL Serostatus:Negative; DENV-1	71.3 (57.2 to 88.9)	82.0 (64.7 to 103.9)		
Parent Trial BL Serostatus:Negative; DENV-2	536.4 (456.9 to 629.6)	410.0 (337.1 to 498.6)		
Parent Trial BL Serostatus:Negative; DENV-3	31.8 (26.3 to 38.5)	26.7 (22.1 to 32.2)		
Parent Trial BL Serostatus:Negative; DENV-4	37.3 (30.7 to 45.4)	24.5 (19.9 to 30.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 2 (Month 12)

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 2 (Month 12)[8]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 2 at Month 12 for participants from both parent trials (DEN-304 and DEN-315). PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses. Number of subjects analysed was variable for each category. '9.99' and '99.9' indicates that the confidence interval was not estimable due to an observed standard deviation of 0.

End point type	Primary

End point timeframe:

Month 12

Notes:

[8] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	48		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial BL Serostatus:Positive; DENV-1	87.2 (37.2 to 204.4)	93.5 (0.0 to 6220000)		
Parent Trial BL Serostatus:Positive; DENV-2	544.5 (279.1 to 1062.4)	272.6 (0.0 to 12600000)		
Parent Trial BL Serostatus:Positive; DENV-3	48.6 (23.2 to 101.6)	34.0 (9.99 to 99.9)		
Parent Trial BL Serostatus:Positive; DENV-4	48.0 (22.2 to 104.0)	21.5 (16.0 to 28.9)		
Parent Trial BL Serostatus:Negative; DENV-1	54.8 (41.7 to 71.9)	96.5 (69.3 to 134.2)		
Parent Trial BL Serostatus:Negative; DENV-2	411.1 (346.6 to 487.6)	276.2 (206.7 to 369.0)		
Parent Trial BL Serostatus:Negative; DENV-3	30.8 (24.8 to 38.2)	25.0 (18.0 to 34.7)		
Parent Trial BL Serostatus:Negative; DENV-4	28.0 (22.7 to 34.5)	23.0 (17.5 to 30.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)[9][10]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 3 at Month 15 for participants from parent trial DEN-304. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Month 15 (DEN-304)

Notes:

[9] - 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: Only descriptive analyses were planned for this endpoint.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-315 was included for this endpoint.

End point values	Prior to Booster: DEN-304			
Subject group type	Reporting group			
Number of subjects analysed	171			
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial BL Serostatus:Positive; DENV-1	214.3 (80.6 to 569.9)			
Parent Trial BL Serostatus:Positive; DENV-2	484.5 (263.4 to 891.3)			
Parent Trial BL Serostatus:Positive; DENV-3	60.4 (29.9 to 122.1)			
Parent Trial BL Serostatus:Positive; DENV-4	58.5 (26.4 to 129.6)			
Parent Trial BL Serostatus:Negative; DENV-1	110.9 (84.9 to 145.0)			
Parent Trial BL Serostatus:Negative; DENV-2	573.6 (483.5 to 680.4)			
Parent Trial BL Serostatus:Negative; DENV-3	37.7 (30.3 to 46.9)			
Parent Trial BL Serostatus:Negative; DENV-4	35.0 (27.7 to 44.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)

End point title	Geometric Mean Titers (GMTs) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)[11][12]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 3 at Month 42 for participants from parent trial DEN-315. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Month 42 (DEN-315)

Notes:

[11] - 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: Only descriptive analyses were planned for this endpoint.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-315 was included for this endpoint.

End point values	Prior to Booster: DEN-315			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus:Positive; DENV-1	320.0 (119.6 to 856.4)			
Parent Trial Baseline Serostatus:Positive; DENV-2	436.6 (156.3 to 1219.1)			
Parent Trial Baseline Serostatus:Positive; DENV-3	80.4 (17.5 to 369.3)			
Parent Trial Baseline Serostatus:Positive; DENV-4	34.7 (5.0 to 242.6)			
Parent Trial Baseline Serostatus:Negative; DENV-1	95.8 (72.2 to 127.2)			
Parent Trial Baseline Serostatus:Negative; DENV-2	188.6 (147.3 to 241.4)			
Parent Trial Baseline Serostatus:Negative; DENV-3	19.3 (15.1 to 24.8)			
Parent Trial Baseline Serostatus:Negative; DENV-4	14.7 (11.5 to 18.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 1 (Month 0 [Day 1])

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 1 (Month 0 [Day 1])[13]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 1 at Month 0 for participants from both parent trials (DEN-304 and DEN-315). PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial.

End point type	Primary

End point timeframe:

Month 0 (Day 1)

Notes:

[13] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	119		
Units: percentage of participants				
number (confidence interval 95%)				

DENV-1	85.8 (80.7 to 89.9)	92.4 (86.1 to 96.5)		
DENV-2	98.7 (96.4 to 99.7)	99.2 (95.4 to 100)		
DENV-3	72.4 (66.3 to 78.0)	79.8 (71.5 to 86.6)		
DENV-4	80.8 (75.2 to 85.6)	76.5 (67.8 to 83.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 2 (Month 12)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 2 (Month 12)[14]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 2 at Month 12 for participants from both parent trials (DEN-304 and DEN-315). PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 12

Notes:

[14] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	48		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	78.6 (71.9 to 84.3)	97.9 (88.9 to 100)		
DENV-2	100 (98.0 to 100)	100 (92.6 to 100)		
DENV-3	72.0 (64.9 to 78.4)	75.0 (60.4 to 86.4)		
DENV-4	76.4 (69.5 to 82.3)	83.3 (69.8 to 92.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 15) (DEN-304)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 15) (DEN-304)[15][16]

End point description:

Seropositivity Rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 3 at Month 15 for participants from parent trial DEN-304. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 15 (DEN-304)

Notes:

[15] - 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: Only descriptive analyses were planned for this endpoint.

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-304 was included for this endpoint.

End point values	Prior to Booster: DEN-304			
Subject group type	Reporting group			
Number of subjects analysed	171			
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	94.2 (89.5 to 97.2)			
DENV-2	99.4 (96.8 to 100)			
DENV-3	81.9 (75.3 to 87.3)			
DENV-4	76.0 (68.9 to 82.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 1 [Month 0 (Day 1])

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 1 [Month 0 (Day 1])[17]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at

baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 1 at Month 0 for participants from both parent trials (DEN-304 and DEN-315). PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 0 (Day 1)

Notes:

[17] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	119		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus:Positive; DENV-1	81.8 (64.5 to 93.0)	100 (63.1 to 100)		
Parent Trial Baseline Serostatus:Positive; DENV-2	97.0 (84.2 to 100)	100 (63.1 to 100)		
Parent Trial Baseline Serostatus:Positive; DENV-3	75.8 (57.7 to 88.9)	100 (63.1 to 100)		
Parent Trial Baseline Serostatus:Positive; DENV-4	87.9 (71.8 to 96.6)	100 (63.1 to 100)		
Parent Trial Baseline Serostatus:Negative; DENV-1	86.4 (81.0 to 90.8)	91.9 (85.2 to 96.2)		
Parent Trial Baseline Serostatus:Negative; DENV-2	99.0 (96.5 to 99.9)	99.1 (95.1 to 100)		
Parent Trial Baseline Serostatus:Negative; DENV-3	71.8 (65.2 to 77.9)	78.4 (69.6 to 85.6)		
Parent Trial Baseline Serostatus:Negative; DENV-4	79.6 (73.5 to 84.9)	74.8 (65.6 to 82.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 2 (Month 12)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 2 (Month 12)[18]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 2 at Month 12 for participants from both parent trials (DEN-304 and DEN-315). PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses. Number of subjects analysed was

variable for each category.

End point type	Primary

End point timeframe:

Month 12

Notes:

[18] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	48		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus:Positive; DENV-1	80.0 (59.3 to 93.2)	100 (15.8 to 100)		
Parent Trial Baseline Serostatus:Positive; DENV-2	100 (86.3 to 100)	100 (15.8 to 100)		
Parent Trial Baseline Serostatus:Positive; DENV-3	76.0 (54.9 to 90.6)	100 (15.8 to 100)		
Parent Trial Baseline Serostatus:Positive; DENV-4	80.0 (59.3 to 93.2)	100 (15.8 to 100)		
Parent Trial Baseline Serostatus:Negative; DENV-1	78.3 (71.1 to 84.5)	97.8 (88.5 to 100)		
Parent Trial Baseline Serostatus:Negative; DENV-2	100 (97.7 to 100)	100 (92.3 to 100)		
Parent Trial Baseline Serostatus:Negative; DENV-3	71.3 (63.6 to 78.3)	73.9 (58.9 to 85.7)		
Parent Trial Baseline Serostatus:Negative; DENV-4	75.8 (68.3 to 82.3)	82.6 (68.6 to 92.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 42) (DEN-315)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 42) (DEN-315)[19][20]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 3 at Month 42 for parent trial DEN-315. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 42 (DEN-315)

Notes:

[19] - 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: Only descriptive analyses were planned for this endpoint.

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-315 was included for this endpoint.

End point values	Prior to Booster: DEN-315			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	96.3 (89.4 to 99.2)			
DENV-2	98.8 (93.2 to 100)			
DENV-3	71.3 (60.0 to 80.8)			
DENV-4	55.0 (43.5 to 66.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)[21][22]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 3 at Month 15 for participants from parent trial DEN-304. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Month 15 (DEN-304)

Notes:

[21] - 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: Only descriptive analyses were planned for this endpoint.

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-304 was included for this endpoint.

End point values	Prior to Booster: DEN-304			
Subject group type	Reporting group			
Number of subjects analysed	171			
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus:Positive; DENV-1	87.5 (67.6 to 97.3)			
Parent Trial Baseline Serostatus:Positive; DENV-2	100 (85.8 to 100)			
Parent Trial Baseline Serostatus:Positive; DENV-3	83.3 (62.6 to 95.3)			
Parent Trial Baseline Serostatus:Positive: DENV-4	79.2 (57.8 to 92.9)			
Parent Trial Baseline Serostatus:Negative: DENV-1	95.2 (90.4 to 98.1)			
Parent Trial Baseline Serostatus:Negative: DENV-2	99.3 (96.3 to 100)			
Parent Trial Baseline Serostatus:Negative: DENV-3	81.6 (74.4 to 87.5)			
Parent Trial Baseline Serostatus:Negative: DENV-4	75.5 (67.7 to 82.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)[23][24]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 3 at Month 42 for parent trial DEN-315. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Month 42 (DEN-315)

Notes:

[23] - 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: Only descriptive analyses were planned for this endpoint.

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-315 was included for this endpoint.

End point values	Prior to Booster: DEN-315			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus:Positive: DENV-1	100 (59.0 to 100)			
Parent Trial Baseline Serostatus:Positive: DENV-2	100 (59.0 to 100)			
Parent Trial Baseline Serostatus:Positive: DENV-3	100 (59.0 to 100)			
Parent Trial Baseline Serostatus:Positive: DENV-4	57.1 (18.4 to 90.1)			
Parent Trial Baseline Serostatus:Negative: DENV-1	95.9 (88.5 to 99.1)			
Parent Trial Baseline Serostatus;Negative: DENV-2	98.6 (92.6 to 100)			
Parent Trial Baseline Serostatus; Negative:DENV-3	68.5 (56.6 to 78.9)			
Parent Trial Baseline Serostatus; Negative:DENV-4	54.8 (42.7 to 66.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster at Visit 1 (Month 0 [Day 1])

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster at Visit 1 (Month 0 [Day 1])[25]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 1 at Month 0 for both parent trials (DEN-304 and DEN-315). PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial.

End point type	Primary

End point timeframe:

Month 0 (Day 1)

Notes:

[25] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	119		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	10.9 (7.2 to 15.5)	9.2 (4.7 to 15.9)		
Trivalent	20.5 (15.6 to 26.2)	18.5 (12.0 to 26.6)		
Tetravalent	61.9 (55.4 to 68.1)	67.2 (58.0 to 75.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster at Visit 2 (Month 12)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster at Visit 2 (Month 12)[26]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 2 at Month 12 for both parent trials (DEN-304 and DEN-315). PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 12

Notes:

[26] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	48		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	12.6 (8.2 to 18.4)	10.4 (3.5 to 22.7)		
Trivalent	21.4 (15.7 to 28.1)	22.9 (12.0 to 37.3)		
Tetravalent	57.1 (49.6 to 64.4)	66.7 (51.6 to 79.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 15) (DEN-304)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 15) (DEN-304)[27][28]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 3 at Month 15 for parent trial DEN-304. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 15 (DEN-304)

Notes:

[27] - 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: Only descriptive analyses were planned for this endpoint.

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-304 was included for this endpoint.

End point values	Prior to Booster: DEN-304			
Subject group type	Reporting group			
Number of subjects analysed	171			
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	10.5 (6.4 to 16.1)			
Trivalent	17.0 (11.7 to 23.4)			
Tetravalent	69.0 (61.5 to 75.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 1 (Month 0 [Day 1])

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 1 (Month 0 [Day 1])[29]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 1 at Month 0 for both parent trials (DEN-304 and DEN-315).PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

Month 0 (Day 1)

Notes:

[29] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	119		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus;Positive: Bivalent	9.1 (1.9 to 24.3)	0 (0.0 to 36.9)		
Parent Trial BL Serostatus;Positive: Trivalent	12.1 (3.4 to 28.2)	0 (0.0 to 36.9)		
Parent Trial BL Serostatus;Positive: Tetravalent	69.7 (51.3 to 84.4)	100 (63.1 to 100)		
Parent Trial BL Serostatus;Negative: Bivalent	11.2 (7.2 to 16.3)	9.9 (5.1 to 17.0)		
Parent Trial BL Serostatus;Negative: Trivalent	21.8 (16.4 to 28.1)	19.8 (12.9 to 28.5)		
Parent Trial BL Serostatus;Negative: Tetravalent	60.7 (53.7 to 67.4)	64.9 (55.2 to 73.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 42) (DEN-315)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster at Visit 3 (Month 42) (DEN-315)[30][31]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4

dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 3 at Month 42 for parent trial DEN-315. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Month 42 (DEN-315)

Notes:

[30] - 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: Only descriptive analyses were planned for this endpoint.

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-315 was included for this endpoint.

End point values	Prior to Booster: DEN-315			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	20.0 (11.9 to 30.4)			
Trivalent	27.5 (18.1 to 38.6)			
Tetravalent	48.8 (37.4 to 60.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 2 (Month 12)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 2 (Month 12)[32]

End point description:

Seropositivity rate for multiple Dengue serotypes:percentage of participants seropositive for more than 1 Dengue serotype,is derived from titers of dengue-neutralizing antibodies.All 4 dengue serotypes(tetravalent),any 2 of 4 dengue serotypes(bivalent),any 3 of 4 dengue serotypes(trivalent).Seropositivity:reciprocal neutralizing titer≥10.Baseline seropositivity:reciprocal neutralizing titer≥10 for one or more dengue serotypes at baseline in parent trial.4 dengue virus serotypes are DENV-1,DENV-2,DENV-3&DENV-4.Reported here is data from Visit 2 at Month12 for both parent trials(DEN-304&DEN-315).PPS:all participants from FAS who received two doses of Takeda's TDV in parent trials with no new major protocol violations in this trial prior to administration of trial vaccination at Visit 3 that could potentially confound primary endpoints in current trial.Subjects analyzed:number of subjects with data available for analyses.Number of subjects analysed:variable for

End point type	Primary

End point timeframe:

Month 12

Notes:

[32] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	182	48		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus;Positive:Bivalent	4.0 (0.1 to 20.4)	0 (0.0 to 84.2)		
Parent Trial BL Serostatus;Positive:Trivalent	20.0 (6.8 to 40.7)	0 (0.0 to 84.2)		
Parent Trial BL Serostatus;Positive:Tetravalent	64.0 (42.5 to 82.0)	100 (15.8 to 100)		
Parent Trial BL Serostatus;Negative:Bivalent	14.0 (9.0 to 20.4)	10.9 (3.6 to 23.6)		
Parent Trial BL Serostatus;Negative: Trivalent	21.7 (15.5 to 28.9)	23.9 (12.6 to 38.8)		
Parent Trial BL Serostatus;Negative: Tetravalent	56.1 (47.9 to 64.0)	65.2 (49.8 to 78.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)[33][34]

End point description:

Seropositivity rate for multiple Dengue serotypes,defined as percentage of participants seropositive for more than 1 Dengue serotype,is derived from titers of dengue-neutralizing antibodies.All 4 dengue serotypes(tetravalent),any 2 of 4 dengue serotypes(bivalent),any 3 of 4 dengue serotypes(trivalent).Seropositivity:as reciprocal neutralizing titer≥10.Baseline seropositivity: as reciprocal neutralizing titer≥10 for one/more dengue serotypes at baseline in parent trial.4 dengue virus serotypes are DENV-1,DENV-2,DENV-3&DENV-4.Reported here is data from Visit3 at Month15 for parent trial DEN-304. PPS:all participants from FAS who received two doses of Takeda's TDV in parent trials with no new major protocol violations in this trial prior to administration of trial vaccination at Visit3 that could potentially confound primary endpoints in current trial.Subjects analysed:number of subjects with data available for analyses.Number of subjects analysed:variable for each category.BL:Baseline.

End point type	Primary

End point timeframe:

Month 15 (DEN-304)

Notes:

[33] - 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: Only descriptive analyses were planned for this endpoint.

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-315 was included for this endpoint.

End point values	Prior to Booster: DEN-304			
Subject group type	Reporting group			
Number of subjects analysed	171			
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus; Positive: Bivalent	8.3 (1.0 to 27.0)			
Parent Trial BL Serostatus; Positive: Trivalent	8.3 (1.0 to 27.0)			
Parent Trial BL Serostatus; Positive: Tetravalent	75.0 (53.3 to 90.2)			
Parent Trial BL Serostatus; Negative: Bivalent	10.9 (6.4 to 17.1)			
Parent Trial BL Serostatus; Negative: Trivalent	18.4 (12.5 to 25.6)			
Parent Trial BL Serostatus; Negative: Tetravalent	68.0 (59.8 to 75.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes in the Period Prior to Booster by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)[35][36]

End point description:

Seropositivity rate for multiple Dengue serotypes,defined as percentage of participants seropositive for more than 1 Dengue serotype,is derived from titers of dengue-neutralizing antibodies.All 4 dengue serotypes(tetravalent),any 2 of 4 dengue serotypes(bivalent),any 3 of 4 dengue serotypes(trivalent).Seropositivity:reciprocal neutralizing titer ≥10.Baseline seropositivity:reciprocal neutralizing titer≥10 for one or more dengue serotypes at baseline in parent trial.4 dengue virus serotypes are DENV-1,DENV-2,DENV-3&DENV-4.Reported here is data from Visit3 at Month42 for parent trial DEN-315.PPS:all participants from FAS who received two doses of Takeda's TDV in parent trials with no new major protocol violations in this trial prior to administration of trial vaccination at Visit 3 that could potentially confound primary endpoints in current trial.Subjects analysed:number of subjects with data available for analyses.Number of subjects analysed was variable for each category.BL:Baseline.

End point type	Primary

End point timeframe:

Month 42 (DEN-315)

Notes:

[35] - 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: Only descriptive analyses were planned for this endpoint.

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only data for participants from parent trial DEN-315 was included for this endpoint.

End point values	Prior to Booster: DEN-315			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus; Positive: Bivalent	0 (0.0 to 41.0)			
Parent Trial BL Serostatus; Positive: Trivalent	42.9 (9.9 to 81.6)			
Parent Trial BL Serostatus; Positive: Tetravalent	57.1 (18.4 to 90.1)			
Parent Trial BL Serostatus; Negative: Bivalent	21.9 (13.1 to 33.1)			
Parent Trial BL Serostatus; Negative: Trivalent	26.0 (16.5 to 37.6)			
Parent Trial BL Serostatus; Negative: Tetravalent	47.9 (36.1 to 60.0)			

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 for Both Parent Trials

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 for Both Parent Trials[37]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 3, pre-booster dose for all participants (Month 15 for parent trial DEN-304 and Month 42 for parent trial DEN-315). Pre-booster dose is defined as the last non-missing value before booster administration. Per Protocol Set-Booster (PPS-B) included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analysed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304) and Month 42 (DEN-315)

Notes:

[37] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	100		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	116.2 (86.6 to 156.0)	120.7 (86.9 to 167.8)		

DENV-2	404.0 (327.2 to 498.8)	361.7 (279.7 to 467.9)		
DENV-3	32.3 (24.8 to 41.9)	30.1 (22.5 to 40.3)		
DENV-4	25.0 (19.0 to 33.0)	26.9 (19.9 to 36.3)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 for Both Parent Trials

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 for Both Parent Trials[38]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 4, 1 month post-booster dose for all participants (Month 16 for parent trial DEN-304 and Month 43 for parent trial DEN-315). PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304) and Month 43 (DEN-315)

Notes:

[38] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	97		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	110.8 (82.2 to 149.5)	1438.3 (1104.0 to 1873.8)		
DENV-2	363.4 (291.8 to 452.7)	1038.8 (833.7 to 1294.4)		
DENV-3	27.7 (21.0 to 36.5)	446.5 (356.8 to 558.8)		
DENV-4	23.6 (17.9 to 31.1)	361.6 (277.6 to 470.9)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 15) (DEN-304)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 15) (DEN-304)[39]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the pre-booster data from Visit 3 at Month 15 for participants from parent trial DEN-304. Pre-booster dose is defined as the last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304)

Notes:

[39] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	61		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	126.4 (82.2 to 194.4)	130.6 (81.9 to 208.4)		
DENV-2	583.9 (448.5 to 760.2)	596.6 (453.4 to 785.1)		
DENV-3	36.9 (26.6 to 51.3)	39.5 (26.3 to 59.6)		
DENV-4	34.1 (23.7 to 49.1)	34.1 (22.3 to 52.1)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 (Month 16) (DEN-304)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 (Month 16) (DEN-304)[40]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 4 at Month 16 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304)

Notes:

[40] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	60		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	120.1 (78.5 to 184.0)	1254.3 (862.2 to 1824.5)		
DENV-2	499.2 (379.7 to 656.4)	1121.4 (867.5 to 1449.5)		
DENV-3	30.6 (21.4 to 43.5)	389.7 (280.8 to 540.8)		
DENV-4	31.0 (21.5 to 44.8)	275.4 (197.8 to 383.6)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 42) (DEN-315)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 42) (DEN-315)[41]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the pre-booster data from Visit 3 at Month 42 for participants from parent trial DEN-315. Pre-booster dose is defined as the last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 42 (DEN-315)

Notes:

[41] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	102.6 (70.6 to 149.0)	106.7 (68.3 to 166.7)		

DENV-2	233.5 (176.1 to 309.8)	165.4 (110.7 to 247.1)		
DENV-3	26.4 (17.0 to 41.1)	19.6 (13.6 to 28.2)		
DENV-4	15.8 (10.6 to 23.5)	18.5 (12.5 to 27.4)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 (Month 43) (DEN-315)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 (Month 43) (DEN-315)[42]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 4 at Month 43 for participants from parent trial DEN-315. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 43 (DEN-315)

Notes:

[42] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	98.4 (65.1 to 148.7)	1795.8 (1273.5 to 2532.5)		
DENV-2	227.5 (164.5 to 314.6)	917.6 (607.2 to 1386.7)		
DENV-3	24.0 (15.2 to 37.8)	556.8 (431.6 to 718.3)		
DENV-4	15.8 (10.6 to 23.5)	562.2 (370.4 to 853.1)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 for Both Parent Trials

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 for Both Parent Trials[43]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 3, pre-booster dose for all participants (Month 15 for parent trial DEN-304 and Month 42 for parent trial DEN-315). Pre-booster dose is defined as the last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304) and Month 42 (DEN-315)

Notes:

[43] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	100		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	165.0 (62.2 to 437.8)	310.4 (67.2 to 1434.4)		
Parent Trial Baseline Serostatus;Positive: DENV-2	353.6 (192.1 to 650.8)	771.3 (334.8 to 1776.9)		
Parent Trial Baseline Serostatus;Positive: DENV-3	53.8 (23.4 to 123.6)	88.8 (25.1 to 313.4)		
Parent Trial Baseline Serostatus;Positive: DENV-4	38.0 (17.4 to 83.3)	57.0 (12.9 to 252.0)		
Parent Trial Baseline Serostatus;Negative: DENV-1	110.4 (80.8 to 150.9)	106.1 (77.2 to 145.9)		
Parent Trial Baseline Serostatus;Negative: DENV-2	411.9 (327.7 to 517.8)	326.2 (249.4 to 426.7)		
Parent Trial Baseline Serostatus;Negative: DENV-3	30.0 (22.7 to 39.6)	26.0 (19.6 to 34.4)		
Parent Trial Baseline Serostatus;Negative: DENV-4	23.5 (17.5 to 31.7)	24.2 (18.2 to 32.3)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 for Both Parent Trials

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 for Both Parent Trials[44]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 4, 1 month post-booster dose for all participants (Month 16 for parent trial DEN-304 and Month 43 for parent trial DEN-315). PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304) and Month 43 (DEN-315)

Notes:

[44] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	97		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	170.5 (59.7 to 487.0)	1192.5 (343.2 to 4143.7)		
Parent Trial Baseline Serostatus;Positive: DENV-2	264.2 (124.8 to 559.2)	1533.3 (720.1 to 3264.5)		
Parent Trial Baseline Serostatus;Positive: DENV-3	46.2 (16.9 to 126.4)	286.5 (124.6 to 658.9)		
Parent Trial Baseline Serostatus;Positive: DENV-4	42.2 (22.7 to 78.4)	243.9 (97.2 to 612.3)		
Parent Trial Baseline Serostatus;Negative: DENV-1	104.4 (76.2 to 143.2)	1473.2 (1129.4 to 1921.6)		
Parent Trial Baseline Serostatus;Negative: DENV-2	379.8 (301.1 to 479.0)	988.3 (783.4 to 1246.9)		
Parent Trial Baseline Serostatus;Negative: DENV-3	25.8 (19.4 to 34.4)	472.6 (374.1 to 597.1)		
Parent Trial Baseline Serostatus;Negative: DENV-4	21.8 (16.1 to 29.5)	380.3 (287.6 to 502.8)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)[45]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the pre-booster data from Visit 3 at Month 15 for participants from parent trial DEN-304. Pre-booster dose is defined as the last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304)

Notes:

[45] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	61		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	120.5 (37.2 to 390.0)	368.4 (44.6 to 3040.1)		
Parent Trial Baseline Serostatus;Positive: DENV-2	368.8 (175.4 to 775.7)	839.4 (298.9 to 2357.3)		
Parent Trial Baseline Serostatus;Positive: DENV-3	39.4 (19.3 to 80.6)	102.1 (19.0 to 549.3)		
Parent Trial Baseline Serostatus;Positive: DENV-4	27.9 (12.9 to 60.2)	79.0 (13.1 to 475.5)		
Parent Trial Baseline Serostatus;Negative: DENV-1	127.6 (79.0 to 206.0)	109.2 (70.2 to 169.7)		
Parent Trial Baseline Serostatus;Negative: DENV-2	639.0 (480.4 to 849.9)	562.4 (423.1 to 747.5)		
Parent Trial Baseline Serostatus;Negative: DENV-3	36.4 (25.0 to 53.2)	33.6 (22.5 to 50.1)		
Parent Trial Baseline Serostatus;Negative: DENV-4	35.5 (23.4 to 53.9)	29.5 (19.5 to 44.6)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 16) (DEN-304)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 16) (DEN-304)[46]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 4 at Month 16 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who

received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304)

Notes:

[46] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	60		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	125.6 (32.3 to 488.7)	1124.7 (182.3 to 6939.8)		
Parent Trial Baseline Serostatus;Positive: DENV-2	264.3 (105.0 to 665.2)	1545.0 (528.1 to 4519.9)		
Parent Trial Baseline Serostatus;Positive: DENV-3	29.3 (11.6 to 74.3)	239.1 (72.7 to 786.1)		
Parent Trial Baseline Serostatus;Positive: DENV-4	32.2 (22.4 to 46.2)	202.8 (57.6 to 714.0)		
Parent Trial Baseline Serostatus;Negative: DENV-1	119.2 (75.0 to 189.3)	1275.5 (879.5 to 1849.6)		
Parent Trial Baseline Serostatus;Negative: DENV-2	559.8 (422.3 to 742.0)	1067.4 (820.0 to 1389.6)		
Parent Trial Baseline Serostatus;Negative: DENV-3	30.8 (20.7 to 45.8)	420.1 (297.4 to 593.5)		
Parent Trial Baseline Serostatus;Negative: DENV-4	30.8 (20.0 to 47.5)	288.7 (203.6 to 409.4)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)[47]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the pre-booster data from Visit 3 at Month 42 for participants from parent trial DEN-315. Pre-booster dose is defined as the last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 42 (DEN-315)

Notes:

[47] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive:DENV-1	470.4 (25.4 to 8709.7)	185.7 (11.7 to 2940.9)		
Parent Trial Baseline Serostatus;Positive:DENV-2	307.1 (19.8 to 4754.2)	598.4 (15.8 to 22694.8)		
Parent Trial Baseline Serostatus;Positive:DENV-3	151.1 (0.7 to 34960.6)	58.2 (1.5 to 2257.4)		
Parent Trial Baseline Serostatus;Positive:DENV-4	107.2 (1.7 to 6684.4)	21.4 (0.0 to 11250.6)		
Parent Trial Baseline Serostatus;Negative:DENV-1	91.0 (63.1 to 131.1)	101.9 (63.5 to 163.5)		
Parent Trial Baseline Serostatus;Negative:DENV-2	228.5 (170.5 to 306.3)	148.6 (99.7 to 221.4)		
Parent Trial Baseline Serostatus;Negative:DENV-3	23.0 (15.2 to 34.8)	17.9 (12.5 to 25.7)		
Parent Trial Baseline Serostatus;Negative:DENV-4	13.5 (9.4 to 19.5)	18.3 (12.6 to 26.6)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 43) (DEN-315)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 43) (DEN-315)[48]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 4 at Month 43 for participants from parent trial DEN-315. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 43 (DEN-315)

Notes:

[48] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive:DENV-1	427.0 (45.4 to 4020.4)	1393.8 (219.3 to 8859.8)		
Parent Trial Baseline Serostatus;Positive:DENV-2	264.1 (8.7 to 8032.8)	1502.5 (236.0 to 9565.9)		
Parent Trial Baseline Serostatus;Positive:DENV-3	180.8 (1.1 to 29718.0)	464.2 (204.7 to 1052.5)		
Parent Trial Baseline Serostatus;Positive:DENV-4	94.8 (1.2 to 7265.6)	398.9 (35.2 to 4522.5)		
Parent Trial Baseline Serostatus;Negative:DENV-1	87.3 (57.6 to 132.5)	1836.5 (1269.6 to 2656.5)		
Parent Trial Baseline Serostatus;Negative:DENV-2	224.8 (160.9 to 314.1)	878.5 (563.9 to 1368.8)		
Parent Trial Baseline Serostatus;Negative:DENV-3	20.4 (13.4 to 31.0)	565.8 (429.2 to 745.8)		
Parent Trial Baseline Serostatus;Negative:DENV-4	13.7 (9.4 to 19.7)	579.4 (370.7 to 905.6)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 for Both Parent Trials

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 for Both Parent Trials[49]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 5, 6 months post-booster dose for all participants (Month 21 for parent trial DEN-304 and Month 48 for parent trial DEN-315). PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304) and Month 48 (DEN-315)

Notes:

[49] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	92		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	94.2 (66.9 to 132.7)	464.9 (336.1 to 642.9)		
DENV-2	305.2 (244.7 to 380.7)	552.5 (442.1 to 690.5)		
DENV-3	27.4 (21.4 to 35.3)	159.5 (122.6 to 207.4)		
DENV-4	20.5 (15.8 to 26.7)	115.4 (85.7 to 155.2)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 (Month 21) (DEN-304)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 (Month 21) (DEN-304)[50]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 5 at Month 21 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304)

Notes:

[50] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	107.8 (65.0 to 179.0)	410.9 (259.7 to 650.1)		
DENV-2	433.0 (321.4 to 583.5)	689.4 (530.6 to 895.8)		
DENV-3	30.7 (21.9 to 42.9)	133.5 (90.5 to 197.0)		
DENV-4	27.3 (18.7 to 39.8)	93.7 (63.7 to 137.8)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 (Month 48) (DEN-315)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 (Month 48) (DEN-315)[51]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Reported here is the data from Visit 5 at Month 48 for participants from parent trial DEN-315. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 48 (DEN-315)

Notes:

[51] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	38		
Units: titer				
geometric mean (confidence interval 95%)				
DENV-1	78.0 (50.6 to 120.2)	553.9 (350.8 to 874.6)		
DENV-2	187.0 (142.3 to 245.6)	403.4 (275.1 to 591.6)		
DENV-3	23.5 (15.9 to 34.6)	205.2 (149.1 to 282.5)		
DENV-4	13.8 (9.9 to 19.2)	155.1 (97.0 to 247.9)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 for Both Parent Trials

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 for Both Parent Trials[52]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 5, 6 month post-booster dose for all participants (Month 21 for parent trial DEN-304 and Month 48 for parent trial DEN-315). PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304) and Month 48 (DEN-315)

Notes:

[52] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	92		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	166.2 (48.3 to 571.7)	435.8 (106.8 to 1777.8)		
Parent Trial Baseline Serostatus;Positive: DENV-2	278.9 (108.9 to 714.1)	699.2 (305.0 to 1603.0)		
Parent Trial Baseline Serostatus;Positive: DENV-3	39.0 (18.8 to 80.8)	137.1 (44.9 to 418.7)		
Parent Trial Baseline Serostatus;Positive: DENV-4	30.2 (15.8 to 57.6)	93.2 (26.8 to 324.4)		
Parent Trial Baseline Serostatus;Negative: DENV-1	88.2 (61.5 to 126.5)	469.4 (338.9 to 650.1)		
Parent Trial Baseline Serostatus;Negative: DENV-2	308.4 (245.1 to 387.9)	533.4 (422.9 to 672.6)		
Parent Trial Baseline Serostatus;Negative: DENV-3	26.3 (20.1 to 34.5)	163.1 (125.1 to 212.7)		
Parent Trial Baseline Serostatus;Negative: DENV-4	19.6 (14.7 to 26.2)	119.1 (88.2 to 160.8)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 21) (DEN-304)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 21) (DEN-304)[53]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1,

DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 5 at Month 21 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304)

Notes:

[53] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	154.2 (30.2 to 786.6)	461.7 (68.8 to 3098.9)		
Parent Trial Baseline Serostatus;Positive: DENV-2	337.6 (104.5 to 1090.2)	825.4 (309.0 to 2205.1)		
Parent Trial Baseline Serostatus;Positive: DENV-3	37.5 (14.4 to 98.0)	145.5 (32.0 to 661.2)		
Parent Trial Baseline Serostatus;Positive: DENV-4	27.5 (12.4 to 61.0)	95.7 (21.6 to 423.2)		
Parent Trial Baseline Serostatus;Negative: DENV-1	101.6 (58.6 to 176.2)	401.4 (254.9 to 632.2)		
Parent Trial Baseline Serostatus;Negative: DENV-2	451.4 (330.8 to 615.9)	665.0 (508.0 to 870.6)		
Parent Trial Baseline Serostatus;Negative: DENV-3	29.7 (20.5 to 43.0)	131.3 (88.3 to 195.1)		
Parent Trial Baseline Serostatus;Negative: DENV-4	27.2 (17.7 to 41.8)	93.3 (62.9 to 138.4)		

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 48) (DEN-315)

End point title	GMTs of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 48) (DEN-315)[54]

End point description:

GMTs of neutralizing antibodies were measured by MNT50 for each of the 4 Dengue Serotypes (DENV-1, DENV-2, DENV-3 and DENV-4). Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. Reported here is the data from Visit 5 at Month 48 for participants from parent trial DEN-315. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of

subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 48 (DEN-315)

Notes:

[54] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	38		
Units: titer				
geometric mean (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive:DENV-1	223.9 (31.8 to 1574.3)	366.4 (8.2 to 16297.5)		
Parent Trial Baseline Serostatus;Positive:DEN-2	129.9 (0.8 to 21199.9)	425.0 (9.5 to 19098.8)		
Parent Trial Baseline Serostatus;Positive:DENV-3	45.5 (6.5 to 319.1)	114.5 (6.0 to 2196.9)		
Parent Trial Baseline Serostatus;Positive:DENV-4	43.9 (0.0 to 55722.2)	86.2 (0.2 to 42114.5)		
Parent Trial Baseline Serostatus;Negative:DENV-1	73.8 (47.1 to 115.6)	573.9 (355.3 to 927.0)		
Parent Trial Baseline Serostatus;Negative:DENV-2	190.6 (143.4 to 253.4)	401.6 (269.9 to 597.6)		
Parent Trial Baseline Serostatus;Negative:DENV-3	22.7 (15.1 to 34.0)	215.7 (155.4 to 299.5)		
Parent Trial Baseline Serostatus;Negative: DENV-4	13.0 (9.3 to 18.1)	163.1 (102.6 to 259.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 for Both Parent Trials

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 for Both Parent Trials[55]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 3, pre-booster dose for all participants (Month 15 for parent trial DEN-304 and Month 42 for parent trial DEN-315). Pre-booster dose is defined as the last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304) and Month 42 (DEN-315)

Notes:

[55] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	100		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	98.0 (93.1 to 99.8)	94.0 (87.4 to 97.8)		
DENV-2	100 (96.4 to 100.0)	99.0 (94.6 to 100.0)		
DENV-3	80.4 (71.4 to 87.6)	73.0 (63.2 to 81.4)		
DENV-4	66.7 (56.6 to 75.7)	67.0 (56.9 to 76.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 for Both Parent Trials

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 for Both Parent Trials[56]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4, 1 month post-booster dose for all participants (Month 16 for parent trial DEN-304 and Month 43 for parent trial DEN-315).PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304) and Month 43 (DEN-315)

Notes:

[56] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	97		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	98.0 (92.9 to 99.8)	100 (96.3 to 100.0)		
DENV-2	100 (96.3 to 100.0)	100 (96.3 to 100.0)		

DENV-3	71.7 (61.8 to 80.3)	100 (96.3 to 100.0)		
DENV-4	66.7 (56.5 to 75.8)	100 (96.3 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 15) (DEN-304)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 15) (DEN-304)[57]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the pre-booster data from Visit 3 at Month 15 for participants from parent trial DEN-304. Pre-booster dose is defined as the last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304)

Notes:

[57] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	61		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	96.7 (88.7 to 99.6)	95.1 (86.3 to 99.0)		
DENV-2	100 (94.1 to 100.0)	100 (94.1 to 100.0)		
DENV-3	83.6 (71.9 to 91.8)	77.0 (64.5 to 86.8)		
DENV-4	75.4 (62.7 to 85.5)	72.1 (59.2 to 82.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 (Month 16) (DEN-304)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 1

	Month Post-Booster Dose at Visit 4 (Month 16) (DEN-304)[58]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4 at Month 16 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304)

Notes:

[58] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	60		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	98.3 (90.9 to 100.0)	100 (94.0 to 100.0)		
DENV-2	100 (93.9 to 100.0)	100 (94.0 to 100.0)		
DENV-3	74.6 (61.6 to 85.0)	100 (94.0 to 100.0)		
DENV-4	76.3 (63.4 to 86.4)	100 (94.0 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 42) (DEN-315)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 42) (DEN-315)[59]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the pre-booster data from Visit 3 at Month 42 for participants from parent trial DEN-315. Pre-booster dose is defined as the last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 42 (DEN-315)

Notes:

[59] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	100 (91.4 to 100.0)	92.3 (79.1 to 98.4)		
DENV-2	100 (91.4 to 100.0)	97.4 (86.5 to 99.9)		
DENV-3	75.6 (59.7 to 87.6)	66.7 (49.8 to 80.9)		
DENV-4	53.7 (37.4 to 69.3)	59.0 (42.1 to 74.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 (Month 43) (DEN-315)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 (Month 43) (DEN-315)[60]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4 at Month 43 for participants from parent trial DEN-315.PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 43 (DEN-315)

Notes:

[60] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	97.5 (86.8 to 99.9)	100 (90.5 to 100.0)		
DENV-2	100 (91.2 to 100.0)	100 (90.5 to 100.0)		

DENV-3	67.5 (50.9 to 81.4)	100 (90.5 to 100.0)		
DENV-4	52.5 (36.1 to 68.5)	100 (90.5 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 for Both Parent Trials

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 for Both Parent Trials[61]

End point description:

Seropositivity rate,defined as percentage of participants seropositive,is derived from titers of dengue-neutralizing antibodies.Seropositivity:reciprocal neutralizing titer ≥10.Baseline seropositivity:reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3&DENV-4. Reported here is data from Visit 3,pre-booster dose for all participants (Month 15 for parent trial DEN-304&Month 42 for parent trial DEN-315).Pre-booster dose is defined as last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304) and Month 42 (DEN-315)

Notes:

[61] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	100		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	92.3 (64.0 to 99.8)	91.7 (61.5 to 99.8)		
Parent Trial Baseline Serostatus;Positive: DENV-2	100 (75.3 to 100.0)	100 (73.5 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-3	92.3 (64.0 to 99.8)	83.3 (51.6 to 97.9)		
Parent Trial Baseline Serostatus;Positive: DENV-4	84.6 (54.6 to 98.1)	66.7 (34.9 to 90.1)		
Parent Trial Baseline Serostatus;Negative: DENV-1	98.9 (93.9 to 100.0)	94.3 (87.2 to 98.1)		
Parent Trial Baseline Serostatus;Negative: DENV-2	100 (95.9 to 100.0)	98.9 (93.8 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-3	78.7 (68.7 to 86.6)	71.6 (61.0 to 80.7)		
Parent Trial Baseline Serostatus;Negative: DENV-4	64.0 (53.2 to 73.9)	67.0 (56.2 to 76.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 for Both Parent Trials

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 for Both Parent Trials[62]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4, 1 month post-booster dose for all participants (Month 16 for parent trial DEN-304 and Month 43 for parent trial DEN-315).PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304) and Month 43 (DEN-315)

Notes:

[62] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	97		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	91.7 (61.5 to 99.8)	100 (71.5 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-2	100 (73.5 to 100.0)	100 (71.5 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-3	83.3 (51.6 to 97.9)	100 (71.5 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-4	100 (73.5 to 100.0)	100 (71.5 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-1	98.9 (93.8 to 100.0)	100 (95.8 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-2	100 (95.8 to 100.0)	100 (95.8 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-3	70.1 (59.4 to 79.5)	100 (95.8 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-4	62.1 (51.0 to 72.3)	100 (95.8 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)[63]

End point description:

Seropositivity rate, defined as percentage of participants seropositive, is derived from titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10.Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 & DENV-4. Reported here is pre-booster data from Visit 3 at Month 15 for participants from parent trial DEN-304. Pre-booster dose is defined as last non-missing value before booster administration.PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304)

Notes:

[63] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	61		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive:DENV-1	90.0 (55.5 to 99.7)	88.9 (51.8 to 99.7)		
Parent Trial Baseline Serostatus;Positive:DENV-2	100 (69.2 to 100.0)	100 (66.4 to 100.0)		
Parent Trial Baseline Serostatus;Positive:DENV-3	90.0 (55.5 to 99.7)	77.8 (40.0 to 97.2)		
Parent Trial Baseline Serostatus;Positive:DENV-4	80.0 (44.4 to 97.5)	77.8 (40.0 to 97.2)		
Parent Trial Baseline Serostatus;Negative:DENV-1	98.0 (89.6 to 100.0)	96.2 (86.8 to 99.5)		
Parent Trial Baseline Serostatus;Negative:DENV-2	100 (93.0 to 100.0)	100 (93.2 to 100.0)		
Parent Trial Baseline Serostatus;Negative:DENV-3	82.4 (69.1 to 91.6)	76.9 (63.2 to 87.5)		
Parent Trial Baseline Serostatus;Negative:DENV-4	74.5 (60.4 to 85.7)	71.2 (56.9 to 82.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 16) (DEN-304)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 16) (DEN-304)[64]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4 at Month 16 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304)

Notes:

[64] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	60		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive:DENV-1	88.9 (51.8 to 99.7)	100 (63.1 to 100.0)		
Parent Trial Baseline Serostatus;Positive:DENV-2	100 (66.4 to 100.0)	100 (63.1 to 100.0)		
Parent Trial Baseline Serostatus;Positive:DENV-3	77.8 (40.0 to 97.2)	100 (63.1 to 100.0)		
Parent Trial Baseline Serostatus;Positive:DENV-4	100 (66.4 to 100.0)	100 (63.1 to 100.0)		
Parent Trial Baseline Serostatus;Negative:DENV-1	100 (92.9 to 100.0)	100 (93.2 to 100.0)		
Parent Trial Baseline Serostatus;Negative:DENV-2	100 (92.9 to 100.0)	100 (93.2 to 100.0)		
Parent Trial Baseline Serostatus;Negative:DENV-3	74.0 (59.7 to 85.4)	100 (93.2 to 100.0)		
Parent Trial Baseline Serostatus;Negative:DENV-4	72.0 (57.5 to 83.8)	100 (93.2 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)[65]

End point description:

Seropositivity rate, defined as percentage of participants seropositive, is derived from titers of dengue-neutralizing antibodies.Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 & DENV-4. Reported here is pre-booster data from Visit 3 at Month 42 for participants from parent trial DEN-315. Pre-booster dose is defined as last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 42 (DEN-315)

Notes:

[65] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	100 (29.2 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-2	100 (29.2 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-3	100 (29.2 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-4	100 (29.2 to 100.0)	33.3 (0.8 to 90.6)		
Parent Trial Baseline Serostatus;Negative: DENV-1	100 (90.7 to 100.0)	91.7 (77.5 to 98.2)		
Parent Trial Baseline Serostatus;Negative: DENV-2	100 (90.7 to 100.0)	97.2 (85.5 to 99.9)		
Parent Trial Baseline Serostatus;Negative: DENV-3	73.7 (56.9 to 86.6)	63.9 (46.2 to 79.2)		
Parent Trial Baseline Serostatus;Negative: DENV-4	50.0 (33.4 to 66.6)	61.1 (43.5 to 76.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 43) (DEN-315)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 43) (DEN-315)[66]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4 at Month 43 for participants from parent trial DEN-315. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 43 (DEN-315)

Notes:

[66] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	100 (29.2 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-2	100 (29.2 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-3	100 (29.2 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-4	100 (29.2 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-1	97.3 (85.8 to 99.9)	100 (89.7 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-2	100 (90.5 to 100.0)	100 (89.7 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-3	64.9 (47.5 to 79.8)	100 (89.7 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-4	48.6 (31.9 to 65.6)	100 (89.7 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 for Both Parent Trials

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 for Both Parent Trials[67]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5, 6 month post-booster dose for all participants (Month 21 for parent trial DEN-304 and Month 48 for parent trial DEN-315). PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304) and Month 48 (DEN-315)

Notes:

[67] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	92		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	90.6 (82.9 to 95.6)	96.7 (90.8 to 99.3)		
DENV-2	100 (96.2 to 100.0)	100 (96.1 to 100.0)		
DENV-3	76.0 (66.3 to 84.2)	98.9 (94.1 to 100.0)		
DENV-4	63.5 (53.1 to 73.1)	94.6 (87.8 to 98.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 (Month 21) (DEN-304)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 6

	Months Post-Booster Dose at Visit 5 (Month 21) (DEN-304)[68]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5 at Month 21 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304)

Notes:

[68] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	89.3 (78.1 to 96.0)	96.3 (87.3 to 99.5)		
DENV-2	100 (93.6 to 100.0)	100 (93.4 to 100.0)		
DENV-3	78.6 (65.6 to 88.4)	98.1 (90.1 to 100.0)		
DENV-4	71.4 (57.8 to 82.7)	96.3 (87.3 to 99.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 (Month 48) (DEN-315)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose at Visit 5 (Month 48) (DEN-315)[69]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5 at Month 48 for participants from parent trial DEN-315. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 48 (DEN-315)

Notes:

[69] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	38		
Units: percentage of participants				
number (confidence interval 95%)				
DENV-1	92.5 (79.6 to 98.4)	97.4 (86.2 to 99.9)		
DENV-2	100 (91.2 to 100.0)	100 (90.7 to 100.0)		
DENV-3	72.5 (56.1 to 85.4)	100 (90.7 to 100.0)		
DENV-4	52.5 (36.1 to 68.5)	92.1 (78.6 to 98.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 for Both Parent Trials

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 for Both Parent Trials[70]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5, 6 month post-booster dose for all participants (Month 21 for parent trial DEN-304 and Month 48 for parent trial DEN-315). PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304) and Month 48 (DEN-315)

Notes:

[70] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	92		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	90.0 (55.5 to 99.7)	91.7 (61.5 to 99.8)		
Parent Trial Baseline Serostatus;Positive: DENV-2	100 (69.2 to 100.0)	100 (73.5 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-3	90.0 (55.5 to 99.7)	91.7 (61.5 to 99.8)		

Parent Trial Baseline Serostatus;Positive: DENV-4	90.0 (55.5 to 99.7)	83.3 (51.6 to 97.9)		
Parent Trial Baseline Serostatus;Negative: DENV-1	90.7 (82.5 to 95.9)	97.5 (91.3 to 99.7)		
Parent Trial Baseline Serostatus;Negative: DENV-2	100 (95.8 to 100.0)	100 (95.5 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-3	74.4 (63.9 to 83.2)	100 (95.5 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-4	60.5 (49.3 to 70.8)	96.3 (89.4 to 99.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 21) (DEN-304)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 21) (DEN-304)[71]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5 at Month 21 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304)

Notes:

[71] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	87.5 (47.3 to 99.7)	88.9 (51.8 to 99.7)		
Parent Trial Baseline Serostatus;Positive: DENV-2	100 (63.1 to 100.0)	100 (66.4 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-3	87.5 (47.3 to 99.7)	88.9 (51.8 to 99.7)		
Parent Trial Baseline Serostatus;Positive: DENV-4	87.5 (47.3 to 99.7)	88.9 (51.8 to 99.7)		
Parent Trial Baseline Serostatus;Negative: DENV-1	89.6 (77.3 to 96.5)	97.8 (88.2 to 99.9)		

Parent Trial Baseline Serostatus;Negative: DENV-2	100 (92.6 to 100.0)	100 (92.1 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-3	77.1 (62.7 to 88.0)	100 (92.1 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-4	68.8 (53.7 to 81.3)	97.8 (88.2 to 99.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 48) (DEN-315)

End point title	Seropositivity Rate for Each of the 4 Dengue Serotypes at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 48) (DEN-315)[72]

End point description:

Seropositivity rate, defined as the percentage of participants seropositive, is derived from the titers of dengue-neutralizing antibodies. Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5 at Month 48 for participants from parent trial DEN-315. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 48 (DEN-315)

Notes:

[72] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	38		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial Baseline Serostatus;Positive: DENV-1	100 (15.8 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-2	100 (15.8 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-3	100 (15.8 to 100.0)	100 (29.2 to 100.0)		
Parent Trial Baseline Serostatus;Positive: DENV-4	100 (15.8 to 100.0)	66.7 (9.4 to 99.2)		
Parent Trial Baseline Serostatus;Negative: DENV-1	92.1 (78.6 to 98.3)	97.1 (85.1 to 99.9)		
Parent Trial Baseline Serostatus;Negative: DENV-2	100 (90.7 to 100.0)	100 (90.0 to 100.0)		
Parent Trial Baseline Serostatus;Negative: DENV-3	71.1 (54.1 to 84.6)	100 (90.0 to 100.0)		

Parent Trial Baseline Serostatus;Negative: DENV-4	50.0 (33.4 to 66.6)	94.3 (80.8 to 99.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose at Visit 3 for Both Parent Trials

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose at Visit 3 for Both Parent Trials[73]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as percentage of participants seropositive for more than one Dengue serotype,is derived from titers of dengue-neutralizing antibodies.All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1,DENV-2,DENV-3&DENV-4. Reported here is data from Visit 3, pre-booster dose for all participants (Month 15 for parent trial DEN-304 and Month 42 for parent trial DEN-315).Pre-booster dose: last non-missing value before booster administration. PPS-B included all participants from FAS-B who received two doses of Takeda's TDV in parent trials with no new major protocol violations after administration of trial vaccination at Visit 3 that could potentially confound primary endpoints in current trial. Subjects analyzed: number of subjects with data available for analyses.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304) and Month 42 (DEN-315)

Notes:

[73] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	100		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	15.7 (9.2 to 24.2)	16.0 (9.4 to 24.7)		
Trivalent	20.6 (13.2 to 29.7)	20.0 (12.7 to 29.2)		
Tetravalent	62.7 (52.6 to 72.1)	59.0 (48.7 to 68.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 for Both Parent Trials

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 for Both Parent Trials[74]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4, 1 month post-booster dose for all participants (Month 16 for parent trial DEN-304 and Month 43 for parent trial DEN-315). PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304) and Month 43 (DEN-315)

Notes:

[74] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	97		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	18.2 (11.1 to 27.2)	0 (0.0 to 3.7)		
Trivalent	24.2 (16.2 to 33.9)	0 (0.0 to 3.7)		
Tetravalent	56.6 (46.2 to 66.5)	100 (96.3 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 15) (DEN-304)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 15) (DEN-304)[75]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as percentage of participants seropositive for more than one Dengue serotype, is derived from titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of 4 dengue serotypes (bivalent), any 3 of 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 & DENV-4. Reported here is pre-booster data from Visit 3 at Month 15 for participants from parent trial DEN-304. Pre-booster dose is defined as last non-missing value before booster administration.PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304)

Notes:

[75] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	61		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	11.5 (4.7 to 22.2)	14.8 (7.0 to 26.2)		
Trivalent	16.4 (8.2 to 28.1)	16.4 (8.2 to 28.1)		
Tetravalent	70.5 (57.4 to 81.5)	65.6 (52.3 to 77.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 (Month 16) (DEN-304)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose at Visit 4 (Month 16) (DEN-304)[76]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4 at Month 16 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304.)

Notes:

[76] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	60		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	15.3 (7.2 to 27.0)	0 (0.0 to 6.0)		
Trivalent	20.3 (11.0 to 32.8)	0 (0.0 to 6.0)		

Tetravalent	64.4 (50.9 to 76.4)	100 (94.0 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 42) (DEN-315)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose at Visit 3 (Month 42) (DEN-315)[77]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as percentage of participants seropositive for more than one Dengue serotype, is derived from titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of 4 dengue serotypes (bivalent), any 3 of 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3&DENV-4. Reported here is pre-booster data from Visit 3 at Month 42 for participants from parent trial DEN-315. Pre-booster dose is defined as last non-missing value before booster administration. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 42 (DEN-315)

Notes:

[77] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	22.0 (10.6 to 37.6)	17.9 (7.5 to 33.5)		
Trivalent	26.8 (14.2 to 42.9)	25.6 (13.0 to 42.1)		
Tetravalent	51.2 (35.1 to 67.1)	48.7 (32.4 to 65.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 1 Month Post-Booster Dose at Visit 4 (Month 43) (DEN-315)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 1 Month Post-Booster Dose at Visit 4

	(Month 43) (DEN-315)[78]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4 at Month 43 for participants from parent trial DEN-315. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 43 (DEN-315)

Notes:

[78] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	22.5 (10.8 to 38.5)	0 (0.0 to 9.5)		
Trivalent	30.0 (16.6 to 46.5)	0 (0.0 to 9.5)		
Tetravalent	45.0 (29.3 to 61.5)	100 (90.5 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 for Both Parent Trials

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 for Both Parent Trials[79]

End point description:

Seropositivity rate for multiple Dengue serotypes,defined as percentage of participants seropositive for more than 1 Dengue serotype,is derived from titers of dengue-neutralizing antibodies.All 4 dengue serotypes(tetravalent),any 2 of 4 dengue serotypes (bivalent),any 3 of 4 dengue serotypes(trivalent).Seropositivity:reciprocal neutralizing titer≥10.Baseline seropositivity:reciprocal neutralizing titer≥10 for one/more dengue serotypes at baseline in parent trial.4 dengue virus serotypes are DENV-1,DENV-2,DENV-3&DENV-4.Reported here is data from Visit 3,pre-booster dose for all participants(Month15 for parent trial DEN-304&Month42 for parent trial DEN-315). Pre-booster dose is defined as last non-missing value before booster administration. Analysis Population: PPS-B. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304) and Month 42 (DEN-315)

Notes:

[79] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	100		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus: Positive; Bivalent	7.7 (0.2 to 36.0)	8.3 (0.2 to 38.5)		
Parent Trial BL Serostatus: Positive; Trivalent	15.4 (1.9 to 45.4)	16.7 (2.1 to 48.4)		
Parent Trial BL Serostatus:Positive;Tetravalent	76.9 (46.2 to 95.0)	66.7 (34.9 to 90.1)		
Parent Trial BL Serostatus: Negative; Bivalent	16.9 (9.8 to 26.3)	17.0 (9.9 to 26.6)		
Parent Trial BL Serostatus: Negative; Trivalent	21.3 (13.4 to 31.3)	20.5 (12.6 to 30.4)		
Parent Trial BL Serostatus:Negative;Tetravalent	60.7 (49.7 to 70.9)	58.0 (47.0 to 68.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 for Both Parent Trials

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 for Both Parent Trials[80]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4, 1 month post-booster dose for all participants (Month 16 for parent trial DEN-304 and Month 43 for parent trial DEN-315). Analysis Population: PPS-B. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304) and Month 43 (DEN-315)

Notes:

[80] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	97		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus: Positive; Bivalent	8.3 (0.2 to 38.5)	0 (0.0 to 28.5)		
Parent Trial BL Serostatus: Positive; Trivalent	8.3 (0.2 to 38.5)	0 (0.0 to 28.5)		
Parent Trial BL Serostatus: Positive; Tetravalent	83.3 (51.6 to 97.9)	100 (71.5 to 100.0)		
Parent Trial BL Serostatus: Negative; Bivalent	19.5 (11.8 to 29.4)	0 (0.0 to 4.2)		
Parent Trial BL Serostatus: Negative; Trivalent	26.4 (17.6 to 37.0)	0 (0.0 to 4.2)		
Parent Trial BL Serostatus: Negative; Tetravalent	52.9 (41.9 to 63.7)	100 (95.8 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 15) (DEN-304)[81]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the pre-booster data from Visit 3 at Month 15 for participants from parent trial DEN-304. Pre-booster dose is defined as the last non-missing value before booster administration. Analysis Population: PPS-B. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 15 (DEN-304)

Notes:

[81] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	61		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus: Positive; Bivalent	10.0 (0.3 to 44.5)	11.1 (0.3 to 48.2)		

Parent Trial BL Serostatus: Positive; Trivalent	20.0 (2.5 to 55.6)	0 (0.0 to 33.6)		
Parent Trial BL Serostatus:Positive;Tetravalent	70.0 (34.8 to 93.3)	77.8 (40.0 to 97.2)		
Parent Trial BL Serostatus: Negative; Bivalent	11.8 (4.4 to 23.9)	15.4 (6.9 to 28.1)		
Parent Trial BL Serostatus: Negative; Trivalent	15.7 (7.0 to 28.6)	19.2 (9.6 to 32.5)		
Parent Trial BL Serostatus:Negative;Tetravalent	70.6 (56.2 to 82.5)	63.5 (49.0 to 76.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 16) (DEN-304)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 16) (DEN-304)[82]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), \any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4 at Month 16 for participants from parent trial DEN-304. Analysis Population: PPS-B. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 16 (DEN-304)

Notes:

[82] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	60		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus: Positive; Bivalent	11.1 (0.3 to 48.2)	0 (0.0 to 36.9)		
Parent Trial BL Serostatus: Positive; Trivalent	11.1 (0.3 to 48.2)	0 (0.0 to 36.9)		
Parent Trial BL Serostatus: Positive; Tetravalent	77.8 (40.0 to 97.2)	100 (63.1 to 100.0)		
Parent Trial BL Serostatus: Negative; Bivalent	16.0 (7.2 to 29.1)	0 (0.0 to 6.8)		
Parent Trial BL Serostatus: Negative; Trivalent	22.0 (11.5 to 36.0)	0 (0.0 to 6.8)		
Parent Trial BL Serostatus: Negative; Tetravalent	62.0 (47.2 to 75.3)	100 (93.2 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at Pre-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 3 (Month 42) (DEN-315)[83]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the pre-booster data from Visit 3 at Month 42 for participants from parent trial DEN-315. Pre-booster dose is defined as the last non-missing value before booster administration. Analysis Population: PPS-B. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

Pre-booster dose at Month 42 (DEN-315)

Notes:

[83] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus: Positive; Bivalent	0 (0.0 to 70.8)	0 (0.0 to 70.8)		
Parent Trial BL Serostatus: Positive; Trivalent	0 (0.0 to 70.8)	66.7 (9.4 to 99.2)		
Parent Trial BL Serostatus: Positive; Tetravalent	100 (29.2 to 100.0)	33.3 (0.8 to 90.6)		
Parent Trial BL Serostatus: Negative; Bivalent	23.7 (11.4 to 40.2)	19.4 (8.2 to 36.0)		
Parent Trial BL Serostatus: Negative; Trivalent	28.9 (15.4 to 45.9)	22.2 (10.1 to 39.2)		
Parent Trial BL Serostatus: Negative; Tetravalent	47.4 (31.0 to 64.2)	50.0 (32.9 to 67.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 43) (DEN-315)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes at 1 Month Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 4 (Month 43) (DEN-315)[84]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 4 at Month 43 for participants from parent trial DEN-315. Analysis Population: PPS-B. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

1 month post-booster dose at Month 43 (DEN-315)

Notes:

[84] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	37		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus: Positive; Bivalent	0 (0.0 to 70.8)	0 (0.0 to 70.8)		
Parent Trial BL Serostatus: Positive; Trivalent	0 (0.0 to 70.8)	0 (0.0 to 70.8)		
Parent Trial BL Serostatus: Positive; Tetravalent	100 (29.2 to 100.0)	100 (29.2 to 100.0)		
Parent Trial BL Serostatus: Negative; Bivalent	24.3 (11.8 to 41.2)	0 (0.0 to 10.3)		
Parent Trial BL Serostatus: Negative; Trivalent	32.4 (18.0 to 49.8)	0 (0.0 to 10.3)		
Parent Trial BL Serostatus: Negative; Tetravalent	40.5 (24.8 to 57.9)	100 (89.7 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 6 Months Post-Booster Dose at Visit 5 for Both Parent Trials

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 6 Months Post-Booster Dose at Visit 5 for Both Parent Trials[85]

End point description:

Seropositivity rate for multiple Dengue serotypes,defined as percentage of participants seropositive for more than one Dengue serotype,is derived from titers of dengue-neutralizing antibodies.All 4 dengue serotypes(tetravalent),any 2 of 4 dengue serotypes (bivalent),any 3 of 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10.4 dengue virus serotypes are DENV-1,DENV-2,DENV-3&DENV-4.Reported here is data from Visit 5, 6 month post-booster dose for all participants(Month 21 for parent trial DEN-304&Month 48 for parent trial DEN-315).PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304) and Month 48 (DEN-315)

Notes:

[85] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	92		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	14.6 (8.2 to 23.3)	2.2 (0.3 to 7.6)		
Trivalent	21.9 (14.1 to 31.5)	5.4 (1.8 to 12.2)		
Tetravalent	57.3 (46.8 to 67.3)	92.4 (84.9 to 96.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 6 Months Post-Booster Dose at Visit 5 (Month 21) (DEN-304)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 6 Months Post-Booster Dose at Visit 5 (Month 21) (DEN-304)[86]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5 at Month 21 for participants from parent trial DEN-304. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304)

Notes:

[86] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	14.3 (6.4 to 26.2)	1.9 (0.0 to 9.9)		
Trivalent	16.1 (7.6 to 28.3)	5.6 (1.2 to 15.4)		
Tetravalent	64.3 (50.4 to 76.6)	92.6 (82.1 to 97.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-booster Dose at 6 Months Post-Booster Dose at Visit 5 (Month 48) (DEN-315)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-booster Dose at 6 Months Post-Booster Dose at Visit 5 (Month 48) (DEN-315)[87]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5 at Month 48 for participants from parent trial DEN-315. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Primary

End point timeframe:

6 months post-Booster dose at Month 48 (DEN-315)

Notes:

[87] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	38		
Units: percentage of participants				
number (confidence interval 95%)				
Bivalent	15.0 (5.7 to 29.8)	2.6 (0.1 to 13.8)		

Trivalent	30.0 (16.6 to 46.5)	5.3 (0.6 to 17.7)		
Tetravalent	47.5 (31.5 to 63.9)	92.1 (78.6 to 98.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 for Both Parent Trials

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 for Both Parent Trials[88]

End point description:

Seropositivity rate for multiple Dengue serotypes,defined as percentage of participants seropositive for more than 1 Dengue serotype, is derived from titers of dengue-neutralizing antibodies.All 4 dengue serotypes (tetravalent),any 2 of 4 dengue serotypes bivalent),any 3 of 4 dengue serotypes(trivalent).Seropositivity:reciprocal neutralizing titer ≥10.Baseline seropositivity: reciprocal neutralizing titer ≥10 for one/more dengue serotypes at baseline in the parent trial. 4 dengue virus serotypes are DENV-1,DENV-2,DENV-3&DENV-4.Reported here is data from Visit 5, 6 month post-booster dose for all participants (Month 21 for parent trial DEN-304 and Month 48 for parent trial DEN-315). Analysis Population: PPS-B. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304) and Month 48 (DEN-315)

Notes:

[88] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	92		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus: Positive; Bivalent	0 (0.0 to 30.8)	8.3 (0.2 to 38.5)		
Parent Trial BL Serostatus: Positive; Trivalent	0 (0.0 to 30.8)	16.7 (2.1 to 48.4)		
Parent Trial BL Serostatus: Positive; Tetravalent	90.0 (55.5 to 99.7)	75.0 (42.8 to 94.5)		
Parent Trial BL Serostatus: Negative; Bivalent	16.3 (9.2 to 25.8)	1.3 (0.0 to 6.8)		
Parent Trial BL Serostatus: Negative; Trivalent	24.4 (15.8 to 34.9)	3.8 (0.8 to 10.6)		
Parent Trial BL Serostatus: Negative; Tetravalent	53.5 (42.4 to 64.3)	95.0 (87.7 to 98.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 21) (DEN-304)

End point title	Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-Booster Dose at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 21) (DEN-304)[89]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5 at Month 21 for participants from parent trial DEN-304. Analysis Population: PPS-B. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

6 months post-booster dose at Month 21 (DEN-304)

Notes:

[89] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	54		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus: Positive; Bivalent	0 (0.0 to 36.9)	11.1 (0.3 to 48.2)		
Parent Trial BL Serostatus: Positive; Trivalent	0 (0.0 to 36.9)	11.1 (0.3 to 48.2)		
Parent Trial BL Serostatus: Positive; Tetravalent	87.5 (47.3 to 99.7)	77.8 (40.0 to 97.2)		
Parent Trial BL Serostatus: Negative; Bivalent	16.7 (7.5 to 30.2)	0 (0.0 to 7.9)		
Parent Trial BL Serostatus: Negative; Tetravalent	60.4 (45.3 to 74.2)	95.6 (84.9 to 99.5)		
Parent Trial BL Serostatus: Negative; Trivalent	18.8 (8.9 to 32.6)	4.4 (0.5 to 15.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Seropositivity Rate for Multiple (2, 3 or 4) Dengue Serotypes Post-booster Dose at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 48) (DEN-315)

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

	Post-booster Dose at 6 Months Post-Booster Dose by Serostatus at Baseline in the Parent Trials at Visit 5 (Month 48) (DEN-315)[90]

End point description:

Seropositivity rate for multiple Dengue serotypes, defined as the percentage of participants seropositive for more than one Dengue serotype, is derived from the titers of dengue-neutralizing antibodies. All 4 dengue serotypes (tetravalent), any 2 of the 4 dengue serotypes (bivalent), any 3 of the 4 dengue serotypes (trivalent). Seropositivity is defined as a reciprocal neutralizing titer ≥10. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. The 4 dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Reported here is the data from Visit 5 at Month 48 for participants from parent trial DEN-315. Analysis Population: PPS-B. Subjects analyzed: number of participants with data available for analyses. Number of subjects analysed was variable for each category. 'BL' indicates Baseline.

End point type	Primary

End point timeframe:

6 months post-Booster dose at Month 48 (DEN-315)

Notes:

[90] - 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: Only descriptive analyses were planned for this endpoint.

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	38		
Units: percentage of participants				
number (confidence interval 95%)				
Parent Trial BL Serostatus: Positive; Bivalent	0 (0.0 to 84.2)	0 (0.0 to 70.8)		
Parent Trial BL Serostatus: Positive; Trivalent	0 (0.0 to 84.2)	33.3 (0.8 to 90.6)		
Parent Trial BL Serostatus:Positive;Tetravalent	100 (15.8 to 100.0)	66.7 (9.4 to 99.2)		
Parent Trial BL Serostatus: Negative; Bivalent	15.8 (6.0 to 31.3)	2.9 (0.1 to 14.9)		
Parent Trial BL Serostatus: Negative; Trivalent	31.6 (17.5 to 48.7)	2.9 (0.1 to 14.9)		
Parent Trial BL Serostatus:Negative;Tetravalent	44.7 (28.6 to 61.7)	94.3 (80.8 to 99.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Ratio (GMR) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes for all Participants Prior to the Booster Dose

End point title	Geometric Mean Ratio (GMR) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes for all Participants Prior to the Booster Dose

End point description:

The geometric mean ratio is the geometric mean of the ratio of the two visits being compared. PPS included all participants from the FAS who received two doses of Takeda’s TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Number of subjects analysed was variable for each category. 'PT' stands for Parent Trials.'999 'indicates that zero participants were analysed for the specified category.

End point type	Secondary

End point timeframe:

Month 12 vs Month 0, Month 15 (DEN-304) vs parent trial Month 4, Mont 42 (DEN315) vs parent trial Month 4, Month 0 vs parent trial Month 9, Month 12 vs parent trial Month 9

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	119		
Units: unitless ratio				
geometric mean (confidence interval 95%)				
Month 12 vs Month 0: DENV-1	0.753 (0.675 to 0.840)	0.891 (0.741 to 1.071)		
Month 12 vs Month 0: DENV-2	0.698 (0.650 to 0.749)	0.622 (0.548 to 0.705)		
Month 12 vs Month 0: DENV-3	0.864 (0.791 to 0.945)	0.852 (0.668 to 1.088)		
Month 12 vs Month 0: DENV-4	0.691 (0.634 to 0.754)	0.861 (0.708 to 1.046)		
Month 15 (DEN-304) vs PT Month 4: DENV-1	0.438 (0.382 to 0.502)	999 (999 to 999)		
Month 15 (DEN-304) vs PT Month 4: DENV-2	0.159 (0.137 to 0.185)	999 (999 to 999)		
Month 15 (DEN-304) vs PT Month 4: DENV-3	0.275 (0.241 to 0.315)	999 (999 to 999)		
Month 15 (DEN-304) vs PT Month 4: DENV-4	0.238 (0.201 to 0.281)	999 (999 to 999)		
Month 42 (DEN-315) vs PT Month 4: DENV-1	999 (999 to 999)	0.296 (0.240 to 0.366)		
Month 42 (DEN-315) vs PT Month 4: DENV-2	999 (999 to 999)	0.108 (0.089 to 0.130)		
Month 42 (DEN-315) vs PT Month 4: DENV-3	999 (999 to 999)	0.202 (0.162 to 0.252)		
Month 42 (DEN-315) vs PT Month 4: DENV-4	999 (999 to 999)	0.095 (0.076 to 0.118)		
Month 0 vs Parent Trial Month 9: DENV-1	0.529 (0.482 to 0.582)	0.517 (0.455 to 0.587)		
Month 0 vs Parent Trial Month 9: DENV-2	0.396 (0.369 to 0.426)	0.466 (0.415 to 0.522)		
Month 0 vs Parent Trial Month 9: DENV-3	0.440 (0.394 to 0.492)	0.547 (0.477 to 0.629)		
Month 0 vs Parent Trial Month 9: DENV-4	0.577 (0.518 to 0.641)	0.568 (0.504 to 0.641)		
Month 12 vs Parent Trial Month 9: DENV-1	0.415 (0.367 to 0.470)	0.486 (0.377 to 0.627)		
Month 12 vs Parent Trial Month 9: DENV-2	0.265 (0.239 to 0.295)	0.289 (0.238 to 0.351)		
Month 12 vs Parent Trial Month 9: DENV-3	0.407 (0.353 to 0.470)	0.435 (0.336 to 0.562)		
Month 12 vs Parent Trial Month 9: DENV-4	0.385 (0.336 to 0.442)	0.567 (0.431 to 0.745)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Ratio (GMR) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes by Serostatus at Baseline in the Parent Trials Prior to the Booster Dose

End point title	Geometric Mean Ratio (GMR) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes by Serostatus at Baseline in the Parent Trials Prior to the Booster Dose

End point description:

The geometric mean ratio is the geometric mean of the ratio of the two visits being compared. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. PPS included all participants from the FAS who received two doses of Takeda's TDV in the parent trials with no new major protocol violations in this trial prior to administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Number of subjects analysed was variable for each category. 'PT' stands for Parent Trials. 'BL' indicates Baseline. '+ve' indicates positive. 'M' stands for Month. '999 'indicates that zero participants were analysed for the specified category. '-99999' and '99999' indicates that the confidence interval was not estimable due to an observed standard deviation of 0.

End point type	Secondary

End point timeframe:

Month 12 vs Month 0, Month 15 (DEN-304) vs parent trial Month 4, Month 42 (DEN315) vs parent trial Month 4, Month 0 vs parent trial Month 9, Month 12 vs parent trial Month 9

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	119		
Units: unitless ratio				
geometric mean (confidence interval 95%)				
PT BL Serostatus: +ve;M12 vs M0:DENV-1	0.736 (0.556 to 0.974)	0.705 (0.002 to 222.445)		
PT BL Serostatus: +ve;M 12 vs M0:DENV-2	0.756 (0.599 to 0.955)	0.456 (0.056 to 3.733)		
PT BL Serostatus: +ve;M 12 vs M0:DENV-3	0.980 (0.834 to 1.152)	1.000 (-99999 to 99999)		
PT BL Serostatus: +ve;M 12 vs M0:DENV-4	0.736 (0.598 to 0.906)	0.727 (0.064 to 8.280)		
PT BL Serostatus:+ve;M15 (DEN-304)vsPT M4:DENV1	0.506 (0.349 to 0.733)	999 (999 to 999)		
PT BL Serostatus:+ve;M15 (DEN-304)vsPT M4:DENV2	0.164 (0.108 to 0.249)	999 (999 to 999)		
PT BL Serostatus:+ve;M15 (DEN-304)vsPT M4:DENV3	0.350 (0.238 to 0.514)	999 (999 to 999)		
PT BL Serostatus:+ve;M15 (DEN-304)vsPT M4:DENV4	0.221 (0.150 to 0.327)	999 (999 to 999)		
PT BL Serostatus: +ve;M42 (DEN-315) vsPT M4:DENV1	999 (999 to 999)	0.393 (0.155 to 0.998)		
PT BL Serostatus: +ve;M42(DEN-315) vsPT M4:DENV2	999 (999 to 999)	0.164 (0.066 to 0.408)		
PT BL Serostatus: +ve;M42(DEN-315) vsPT M4:DENV-3	999 (999 to 999)	0.319 (0.204 to 0.499)		
PT BL Serostatus: +ve;M42(DEN-315) vsPT M4:DENV-4	999 (999 to 999)	0.104 (0.042 to 0.258)		

PT BL Serostatus: +ve;M0vsPT M9:DENV1	0.635 (0.467 to 0.864)	0.528 (0.453 to 0.616)		
PT BL Serostatus: +ve;M0vs PT M9:DENV2	0.469 (0.356 to 0.619)	0.454 (0.312 to 0.661)		
PT BL Serostatus: +ve;M0 vs PT M9:DENV3	0.538 (0.361 to 0.801)	0.556 (0.356 to 0.868)		
PT BL Serostatus: +ve;M0 vs PT M9: DENV-4	0.710 (0.475 to 1.062)	0.684 (0.401 to 1.165)		
PT BL Serostatus: +ve;M12 vs PT M 9:DENV-1	0.497 (0.330 to 0.748)	0.375 (0.000 to 400.159)		
PT BL Serostatus: +ve;M12 vs PT M 9:DENV-2	0.311 (0.203 to 0.477)	0.172 (0.161 to 0.184)		
PT BL Serostatus: +ve;M12 vs PT M 9:DENV-3	0.561 (0.329 to 0.957)	0.664 (0.004 to 119.652)		
PT BL Serostatus: +ve;M12 vs PT M 9:DENV-4	0.577 (0.335 to 0.994)	0.966 (0.005 to 194.455)		
PT BL Serostatus:-ve;M12 vs M0; DENV-1	0.756 (0.671 to 0.851)	0.900 (0.745 to 1.088)		
PT BL Serostatus:-ve;M12 vs M0; DENV-2	0.689 (0.639 to 0.742)	0.630 (0.553 to 0.718)		
PT BL Serostatus:-ve;M12 vs M0; DENV-3	0.847 (0.767 to 0.936)	0.846 (0.656 to 1.092)		
PT BL Serostatus: -ve;M12 vs M0; DENV-4	0.684 (0.622 to 0.753)	0.867 (0.708 to 1.063)		
PT BL Serostatus:-ve;M15(DEN-304)vsPT M4;DENV1	0.427 (0.368 to 0.496)	999 (999 to 999)		
PT BL Serostatus:-ve;M15(DEN-304)vsPT M4;DENV2	0.158 (0.135 to 0.186)	999 (999 to 999)		
PT BL Serostatus:-ve;M15(DEN-304)vsPT M4;DENV3	0.265 (0.229 to 0.305)	999 (999 to 999)		
PT BL Serostatus:-ve;M15(DEN-304)vsPT M4;DENV4	0.241 (0.200 to 0.290)	999 (999 to 999)		
PT BL Serostatus:-ve;M42(DEN-315)vsPT M4;DENV1	999 (999 to 999)	0.288 (0.231 to 0.359)		
PT BL Serostatus:-ve;M42(DEN-315)vsPT M4;DENV2	999 (999 to 999)	0.103 (0.085 to 0.125)		
PT BL Serostatus:-ve;M42(DEN-315)vsPT M4;DENV3	999 (999 to 999)	0.192 (0.152 to 0.244)		
PT BL Serostatus:-ve;M42(DEN-315)vsPT M4;DENV4	999 (999 to 999)	0.094 (0.075 to 0.118)		
PT BL Serostatus: Negative;M0 vs PT M 9;DENV-1	0.514 (0.466 to 0.567)	0.516 (0.450 to 0.592)		
PT BL Serostatus: Negative;M0 vs PT M9;DENV-2	0.385 (0.359 to 0.414)	0.467 (0.413 to 0.527)		
PT BL Serostatus: Negative;M0 vs PT M9;DENV-3	0.426 (0.381 to 0.477)	0.547 (0.472 to 0.633)		
PT BL Serostatus: Negative;M0 vs PT M9;DENV-4	0.557 (0.501 to 0.619)	0.560 (0.494 to 0.634)		
PT BL Serostatus: Negative;M12 vs PT M9;DENV-1	0.403 (0.354 to 0.459)	0.492 (0.378 to 0.641)		
PT BL Serostatus: Negative;M12 vs PT M9;DENV-2	0.259 (0.233 to 0.287)	0.296 (0.242 to 0.362)		
PT BL Serostatus: Negative;M12 vs PT M9;DENV-3	0.387 (0.335 to 0.446)	0.426 (0.327 to 0.556)		
PT BL Serostatus: Negative;M12 vs PT M9;DENV-4	0.361 (0.316 to 0.412)	0.553 (0.416 to 0.734)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMR of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Booster Phase

End point title	GMR of Neutralizing Antibodies for Each of the 4 Dengue Serotypes in the Booster Phase

End point description:

The geometric mean ratio is the geometric mean of the ratio of the two visits being compared. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Number of subjects analysed was variable for each category.

End point type	Secondary

End point timeframe:

Months (M) 1&6 post-booster dose in current trial vs M 4 in parent trials; post-booster M 6 vs post-booster M 1; post-booster M 1 vs pre-booster (M 15 for DEN-304/M 42 for DEN-315); post-booster M 6 vs pre-booster (M 15 for DEN-304/M 42 for DEN-315)

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	100		
Units: unitless ratio				
geometric mean (confidence interval 95%)				
Booster Month 1 vs Parent Trial Month 4: DENV-1	0.352 (0.296 to 0.417)	4.298 (3.204 to 5.767)		
Booster Month 1 vs Parent Trial Month 4: DENV-2	0.124 (0.107 to 0.144)	0.378 (0.285 to 0.502)		
Booster Month 1 vs Parent Trial Month 4: DENV-3	0.231 (0.188 to 0.284)	3.042 (2.217 to 4.175)		
Booster Month 1 vs Parent Trial Month 4: DENV-4	0.162 (0.127 to 0.206)	1.966 (1.412 to 2.738)		
Booster Month 6 vs Parent Trial Month 4: DENV-1	0.285 (0.235 to 0.345)	1.409 (1.036 to 1.917)		
Booster Month 6 vs Parent Trial Month 4: DENV-2	0.100 (0.086 to 0.117)	0.206 (0.158 to 0.269)		
Booster Month 6 vs Parent Trial Month 4:DENV-3	0.225 (0.187 to 0.272)	1.133 (0.816 to 1.573)		
Booster Month 6 vs Parent Trial Month 4: DENV-4	0.136 (0.110 to 0.169)	0.609 (0.445 to 0.834)		
Booster Month 6 vs Booster Month 1: DENV-1	0.817 (0.730 to 0.914)	0.334 (0.283 to 0.395)		
Booster Month 6 vs Booster Month 1: DENV-2	0.825 (0.753 to 0.903)	0.535 (0.452 to 0.634)		
Booster Month 6 vs Booster Month 1: DENV-3	0.990 (0.894 to 1.096)	0.370 (0.295 to 0.463)		
Booster Month 6 vs Booster Month 1: DENV-4	0.875 (0.746 to 1.026)	0.317 (0.255 to 0.394)		
Booster Month 1 vs Pre-booster dose: DENV-1	0.962 (0.879 to 1.053)	11.762 (8.660 to 15.975)		
Booster Month 1 vs Pre-booster dose: DENV-2	0.936 (0.862 to 1.016)	2.822 (2.208 to 3.607)		
Booster Month 1 vs Pre-booster dose: DENV-3	0.856 (0.773 to 0.948)	14.889 (10.992 to 20.170)		

Booster Month 1 vs Pre-booster dose: DENV-4	0.960 (0.816 to 1.130)	13.890 (9.549 to 20.204)		
Booster Month 6 vs Pre-booster dose: DENV-1	0.784 (0.699 to 0.879)	3.810 (2.847 to 5.097)		
Booster Month 6 vs Pre-booster dose: DENV-2	0.763 (0.697 to 0.835)	1.550 (1.250 to 1.923)		
Booster Month 6 vs Pre-booster dose: DENV-3	0.858 (0.767 to 0.960)	5.622 (4.151 to 7.614)		
Booster Month 6 vs Pre-booster dose: DENV-4	0.834 (0.708 to 0.983)	4.412 (3.187 to 6.108)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMR of Neutralizing Antibodies for Each of the 4 Dengue Serotypes by Serostatus at Baseline in the Parent Trials in the Booster Phase

End point title	GMR of Neutralizing Antibodies for Each of the 4 Dengue Serotypes by Serostatus at Baseline in the Parent Trials in the Booster Phase

End point description:

The geometric mean ratio is the geometric mean of the ratio of the two visits being compared. Baseline seropositivity is defined as reciprocal neutralizing titer ≥10 for one or more dengue serotypes at baseline in the parent trial. PPS-B included all participants from the FAS-B who received two doses of Takeda's TDV in the parent trials with no new major protocol violations after administration of the trial vaccination at Visit 3 that could potentially confound the primary endpoints in the current trial. Number of subjects analysed was variable for each category. 'PT' stands for Parent Trials. 'BL' indicates Baseline. '+ve' indicates positive. '-ve' indicates negative. 'M' stands for Month.

End point type	Secondary

End point timeframe:

Months (M) 1&6 post-booster dose in current trial vs M 4 in parent trials; post-booster M 1 vs pre-booster (M 15 for DEN-304/M 42 for DEN-315); post-booster M 6 vs pre-booster (M 15 for DEN-304/M 42 for DEN-315); post-booster M 6 vs post-booster M 1

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	100		
Units: unitless ratio				
geometric mean (confidence interval 95%)				
PT BL Serostatus:+ve;Booster M1 vs PT M4:DENV-1	0.413 (0.236 to 0.721)	2.219 (1.181 to 4.169)		
PT BL Serostatus:+ve;Booster M1 vs PT M4:DENV-2	0.118 (0.077 to 0.180)	0.355 (0.203 to 0.620)		
PT BL Serostatus:+ve;Booster M1 vs PT M4:DENV-3	0.311 (0.186 to 0.520)	1.566 (0.684 to 3.583)		
PT BL Serostatus:+ve;Booster M1 vs PT M4:DENV-4	0.229 (0.144 to 0.363)	1.215 (0.662 to 2.231)		
PT BL Serostatus:+ve;Booster M1vsPrebooster:DENV1	1.033 (0.833 to 1.280)	3.683 (1.612 to 8.412)		
PT BL Serostatus:+ve;Booster M1vsPrebooster:DENV2	0.803 (0.615 to 1.049)	1.805 (1.311 to 2.485)		

PT BL Serostatus:+ve;Booster M1vsPrebooster:DENV3	0.825 (0.580 to 1.174)	3.699 (1.738 to 7.873)		
PT BL Serostatus:+ve;Booster M1vsPrebooster:DENV4	1.203 (0.681 to 2.126)	5.237 (1.977 to 13.872)		
PT BL Serostatus:+ve;Booster M6vsPrebooster:DENV1	1.065 (0.673 to 1.686)	1.404 (0.787 to 2.506)		
PT BL Serostatus:+ve;Booster M6vsPrebooster:DENV2	0.739 (0.480 to 1.137)	0.906 (0.673 to 1.221)		
PT BL Serostatus:+ve;Booster M6vsPrebooster:DENV3	0.965 (0.733 to 1.271)	1.544 (0.868 to 2.748)		
PT BL Serostatus:+ve;Booster M6vsPrebooster:DENV4	0.903 (0.513 to 1.588)	1.635 (0.724 to 3.690)		
PT BL Serostatus:+ve;Booster M6vsBooster M1:DENV1	0.998 (0.742 to 1.343)	0.379 (0.221 to 0.650)		
PT BL Serostatus:+ve;Booster M6vsBooster M1:DENV2	1.026 (0.713 to 1.475)	0.506 (0.330 to 0.775)		
PT BL Serostatus:+ve;Booster M6vsBooster M1:DENV3	1.024 (0.821 to 1.278)	0.437 (0.255 to 0.750)		
PT BL Serostatus:+ve;Booster M6vsBooster M1:DENV4	0.837 (0.492 to 1.425)	0.329 (0.173 to 0.624)		
PT BL Serostatus:+ve;Booster M6vsPT M4:DENV1	0.400 (0.175 to 0.915)	0.779 (0.379 to 1.599)		
PT BL Serostatus:+ve;Booster M6vsPT M4:DENV2	0.103 (0.066 to 0.162)	0.161 (0.086 to 0.304)		
PT BL Serostatus:+ve;Booster M6vsPT M4:DENV3	0.333 (0.215 to 0.515)	0.593 (0.267 to 1.321)		
PT BL Serostatus:+ve;Booster M6vsPT M4:DENV4	0.113 (0.063 to 0.201)	0.314 (0.134 to 0.735)		
PT BL Serostatus:-ve;Booster M1vsPT M4;DENV1	0.343 (0.286 to 0.413)	4.692 (3.404 to 6.467)		
PT BL Serostatus:-ve;Booster M1vsPT M4;DENV2	0.125 (0.106 to 0.147)	0.382 (0.278 to 0.523)		
PT BL Serostatus:-ve;Booster M1vsPT M4;DENV3	0.221 (0.177 to 0.277)	3.322 (2.359 to 4.678)		
PT BL Serostatus:-ve;Booster M1vsPT M4;DENV4	0.130 (0.099 to 0.171)	1.585 (1.112 to 2.259)		
PT BL Serostatus:-ve;Booster M1vsPrebooster;DENV1	0.953 (0.862 to 1.053)	13.646 (9.906 to 18.796)		
PT BL Serostatus:-ve;Booster M1vsPrebooster;DENV2	0.956 (0.876 to 1.043)	2.988 (2.275 to 3.925)		
PT BL Serostatus:-ve;Booster M1vsPrebooster;DENV3	0.860 (0.771 to 0.959)	17.792 (13.012 to 24.329)		
PT BL Serostatus:-ve;Booster M1vsPrebooster;DENV4	0.939 (0.820 to 1.074)	14.586 (10.186 to 20.888)		
PT BL Serostatus:-ve;Booster M6vsPrebooster;DENV1	0.756 (0.672 to 0.851)	4.425 (3.233 to 6.056)		
PT BL Serostatus:-ve;Booster M6vsPrebooster;DENV2	0.766 (0.698 to 0.840)	1.680 (1.321 to 2.137)		
PT BL Serostatus:-ve;Booster M6vsPrebooster;DENV3	0.846 (0.749 to 0.957)	6.824 (4.957 to 9.395)		
PT BL Serostatus:-ve;Booster M6vsPrebooster;DENV4	0.801 (0.692 to 0.926)	4.837 (3.533 to 6.623)		
PT BL Serostatus:-ve;Booster M6vsBooster M1;DENV1	0.799 (0.709 to 0.902)	0.328 (0.274 to 0.393)		
PT BL Serostatus:-ve;Booster M6vsBooster M1;DENV2	0.805 (0.733 to 0.885)	0.539 (0.447 to 0.650)		
PT BL Serostatus:-ve;Booster M6vsBooster M1;DENV3	0.986 (0.882 to 1.103)	0.361 (0.282 to 0.463)		
PT BL Serostatus:-ve;Booster M6vsBooster M1;DENV4	0.850 (0.746 to 0.969)	0.319 (0.255 to 0.399)		

PT BL Serostatus:-ve;Booster M6vs PT M4;DENV1	0.273 (0.224 to 0.333)	1.546 (1.102 to 2.168)		
PT BL Serostatus:-ve;Booster M6vs PT M4;DENV2	0.100 (0.085 to 0.118)	0.214 (0.160 to 0.288)		
PT BL Serostatus:-ve;Booster M6vs PT M4;DENV3	0.215 (0.175 to 0.263)	1.253 (0.875 to 1.795)		
PT BL Serostatus:-ve;Booster M6vs PT M4;DENV4	0.109 (0.086 to 0.139)	0.498 (0.357 to 0.694)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Solicited Local (Injection Site) Adverse Events (AEs) within 7 Days Post-Booster Vaccination

End point title	Percentage of Participants With Solicited Local (Injection Site) Adverse Events (AEs) within 7 Days Post-Booster Vaccination

End point description:

Solicited local AEs at injection site are defined as pain, erythema and swelling that occurred within 7 days post-booster dose at Month 15 (DEN-304) and Month 42 (DEN-315). AEs were graded by the investigator in the following manner: Mild: Grade 1: Awareness of symptoms that are easily tolerated, causing minimal discomfort and not interfering with everyday activities. Relieved with or without symptomatic treatment; Moderate: Grade 2: Sufficient discomfort is present to cause interference with normal activity.Only partially relieved with symptomatic treatment; Severe: Grade 3: Extreme distress, causing significant impairment of functioning or incapacitation. Prevents normal everyday activities. Not relieved with symptomatic treatment.Safety Set-Booster (SAF-B) included all participants who received at least one dose of Takeda's TDV in the parent trials and who received the trial vaccination in the current trial.Subjects analyzed: number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Days 1 through 7 post-booster dose at Visit 3 (Month 15 [DEN-304]) and (Month 42 [DEN-315])

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	112		
Units: percentage of participants				
number (not applicable)				
Mild	17.4	50.0		
Moderate	5.2	14.3		
Severe	0	1.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with any Serious Adverse Events (SAEs) Prior to the Booster Dose

End point title	Percentage of Participants with any Serious Adverse Events

	(SAEs) Prior to the Booster Dose

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a trial vaccine or placebo; it does not necessarily have to have a causal relationship with this treatment. An SAE is defined as any untoward medical occurrence or effect that at any dose 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 event. SAF included all participants who agreed to participate in the current trial, did not screen fail, and who received at least one dose of Takeda's TDV in the parent trials.

End point type	Secondary

End point timeframe:

Month 0 through Month 15 (DEN-304) and Month 42 (DEN-315)

End point values	Prior to Booster: DEN-304	Prior to Booster: DEN-315		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	119		
Units: percentage of participants				
number (not applicable)	2.4	6.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Solicited Systemic Adverse Events within 14 Days Post-Booster Vaccination by Severity

End point title	Percentage of Participants With Solicited Systemic Adverse Events within 14 Days Post-Booster Vaccination by Severity

End point description:

Solicited systemic AEs are defined as fever, headache, asthenia, malaise and myalgia that occurred within 14 days post-booster dose at Month 15 (DEN-304) and Month 42 (DEN-315). AEs were graded by the investigator in the following manner: Mild: Grade 1: Awareness of symptoms that are easily tolerated, causing minimal discomfort and not interfering with everyday activities. Relieved with or without symptomatic treatment; Moderate: Grade 2: Sufficient discomfort is present to cause interference with normal activity. Only partially relieved with symptomatic treatment; Severe: Grade 3: Extreme distress, causing significant impairment of functioning or incapacitation. Prevents normal everyday activities. Not relieved with symptomatic treatment. SAF-B included all participants who received at least one dose of Takeda's TDV in the parent trials and who received the trial vaccination in the current trial. Subjects analyzed: number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

Days 1 through 14 post-booster dose at Visit 3 (Month 15 [DEN-304]) and (Month 42 [DEN-315])

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	112		
Units: percentage of participants				
number (not applicable)				
Mild	30.4	32.1		
Moderate	12.2	17.0		
Severe	1.7	3.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with any Medically Attended AEs (MAAEs) in the Booster Phase

End point title	Percentage of Participants with any Medically Attended AEs (MAAEs) in the Booster Phase

End point description:

MAAEs are defined as AEs leading to an unscheduled visit to or by a healthcare professional including visits to an emergency department, but not fulfilling seriousness criteria. SAF-B included all participants who received at least one dose of Takeda’s TDV in the parent trials and who received the trial vaccination in the current trial.

End point type	Secondary

End point timeframe:

Month 15 post-booster dose through Month 21 (DEN-304); Month 42 post-booster dose through Month 48 (DEN-315)

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	115		
Units: percentage of participants				
number (not applicable)	16.9	11.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with any Unsolicited AEs in the Booster Phase

End point title	Percentage of Participants with any Unsolicited AEs in the Booster Phase

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a trial vaccine or placebo; it does not necessarily have to have a causal relationship with this treatment.SAF-B included all participants who received at least one dose of Takeda’s TDV in the parent trials and who received the trial vaccination in the current trial.

End point type	Secondary

End point timeframe:

Days 1 through 28 post-booster dose at Visit 3 (Month 15 [DEN-304]) and (Month 42 [DEN-315])

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	115		
Units: percentage of participants				
number (not applicable)	6.8	6.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with any SAEs in the Booster Phase

End point title	Percentage of Participants with any SAEs in the Booster Phase

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a trial vaccine or placebo; it does not necessarily have to have a causal relationship with this treatment. An SAE is defined as any untoward medical occurrence or effect that at any dose 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 event. SAF-B included all participants who received at least one dose of Takeda’s TDV in the parent trials and who received the trial vaccination in the current trial.

End point type	Secondary

End point timeframe:

Month 15 post-booster dose after vaccination through Month 21 (DEN-304); Month 42 post-booster dose after vaccination through Month 48 (DEN-315)

End point values	Booster Phase: Placebo	Booster Phase: TDV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	115		
Units: percentage of participants				
number (not applicable)	2.5	0		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and SAEs:From Day 1 [Month 0] up to Month 21 (DEN-304), Month 48 (DEN-315); Non-serious adverse events: Up to 28 days (day of vaccination + 27 days) after administration of each vaccine dose on Months 15 (DEN-304), 42 (DEN-315).

Adverse event reporting additional description:

Prior to Booster Arms: SAF included all participants who agreed to participate in current trial,did not screen fail, who received at least 1 dose of Takeda's TDV in parent trials. Booster Phase Arms: SAF-B included all participants who received at least 1 dose of Takeda's TDV in parent trials, who received the trial vaccination in current trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Prior to Booster: DEN-304

Reporting group description:

Participants who received TDV in parent trial DEN-304 (US) were assessed before they received booster dose (Placebo/TDV) at Visit 3 (Month 15).

Reporting group title	Booster Phase: Placebo

Reporting group description:

Participants received TDV placebo-matching 0.5 mL injection, subcutaneously, once at Month 15 for participants from parent trial DEN-304 (US) or once at Month 42 for participants from parent trial DEN-315 (Mexico).

Reporting group title	Booster Phase: TDV

Reporting group description:

Participants received TDV 0.5 mL, injection, subcutaneously, once at Month 15 for participants from parent trials DEN-304 (US) or once at Month 42 for participants from parent trial DEN-315 (Mexico).

Reporting group title	Prior to Booster: DEN-315

Reporting group description:

Participants who received TDV in parent trial DEN-315 (Mexico) were assessed before they received booster dose (Placebo/TDV) at Visit 3 (Month 42).

Serious adverse events	Prior to Booster: DEN-304	Booster Phase: Placebo	Booster Phase: TDV
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 246 (2.44%)	3 / 118 (2.54%)	0 / 115 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Leukaemia			
subjects affected / exposed	0 / 246 (0.00%)	0 / 118 (0.00%)	0 / 115 (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
Breast cancer			

subjects affected / exposed	1 / 246 (0.41%)	0 / 118 (0.00%)	0 / 115 (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
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 246 (0.00%)	1 / 118 (0.85%)	0 / 115 (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
Fall			
subjects affected / exposed	1 / 246 (0.41%)	0 / 118 (0.00%)	0 / 115 (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
Rib fracture			
subjects affected / exposed	1 / 246 (0.41%)	0 / 118 (0.00%)	0 / 115 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 246 (0.00%)	1 / 118 (0.85%)	0 / 115 (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
Acute coronary syndrome			
subjects affected / exposed	1 / 246 (0.41%)	0 / 118 (0.00%)	0 / 115 (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
Pregnancy, puerperium and perinatal conditions			
Uterine atony			
subjects affected / exposed	0 / 246 (0.00%)	0 / 118 (0.00%)	0 / 115 (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
Abortion spontaneous			

subjects affected / exposed	0 / 246 (0.00%)	1 / 118 (0.85%)	0 / 115 (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
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 246 (0.41%)	0 / 118 (0.00%)	0 / 115 (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
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 246 (0.00%)	0 / 118 (0.00%)	0 / 115 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	1 / 246 (0.41%)	0 / 118 (0.00%)	0 / 115 (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
Osteonecrosis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 118 (0.00%)	0 / 115 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 246 (0.41%)	0 / 118 (0.00%)	0 / 115 (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
Mastitis			
subjects affected / exposed	0 / 246 (0.00%)	0 / 118 (0.00%)	0 / 115 (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
Pilonidal disease			

subjects affected / exposed	0 / 246 (0.00%)	0 / 118 (0.00%)	0 / 115 (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
Pneumonia bacterial			
subjects affected / exposed	0 / 246 (0.00%)	0 / 118 (0.00%)	0 / 115 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 246 (0.00%)	0 / 118 (0.00%)	0 / 115 (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

Serious adverse events	Prior to Booster: DEN-315		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 119 (6.72%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Leukaemia			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Breast cancer			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			

subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute coronary syndrome			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Uterine atony			
subjects affected / exposed	2 / 119 (1.68%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychotic disorder			

subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mastitis			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pilonidal disease			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Prior to Booster: DEN-304	Booster Phase: Placebo	Booster Phase: TDV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 246 (0.00%)	57 / 118 (48.31%)	83 / 115 (72.17%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 246 (0.00%)	38 / 118 (32.20%)	42 / 115 (36.52%)
occurrences (all)	0	111	153
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 246 (0.00%)	26 / 118 (22.03%)	70 / 115 (60.87%)
occurrences (all)	0	56	247
Malaise			
subjects affected / exposed	0 / 246 (0.00%)	23 / 118 (19.49%)	28 / 115 (24.35%)
occurrences (all)	0	48	81
Injection site erythema			
subjects affected / exposed	0 / 246 (0.00%)	2 / 118 (1.69%)	8 / 115 (6.96%)
occurrences (all)	0	2	8
Asthenia			
subjects affected / exposed	0 / 246 (0.00%)	22 / 118 (18.64%)	28 / 115 (24.35%)
occurrences (all)	0	49	84
Swelling			
subjects affected / exposed	0 / 246 (0.00%)	0 / 118 (0.00%)	16 / 115 (13.91%)
occurrences (all)	0	0	47
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 246 (0.00%)	0 / 118 (0.00%)	29 / 115 (25.22%)
occurrences (all)	0	0	97
Musculoskeletal and connective tissue disorders			
Myalgia			

subjects affected / exposed	0 / 246 (0.00%)	22 / 118 (18.64%)	40 / 115 (34.78%)
occurrences (all)	0	59	154
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 246 (0.00%)	6 / 118 (5.08%)	5 / 115 (4.35%)
occurrences (all)	0	6	6

Non-serious adverse events	Prior to Booster: DEN-315		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 119 (0.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Injection site erythema			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Swelling			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			

Myalgia subjects affected / exposed occurrences (all)	0 / 119 (0.00%) 0		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 119 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2020	The following change was made as per amendment 01: 1. The booster dose administration schedule was changed from 57 months to 36 months after the first vaccination in the primary vaccination series.
22 February 2021	The following change was made as per amendment 02: 1. The booster dose administration schedule was changed from 36 months to 45 months after the first vaccination in the primary for subjects from parent trial DEN-315 (Mexico).
22 August 2022	The following change was made as per amendment 03: 1. The booster dose administration schedule was changed from 45 months to 63 months after the first vaccination in the primary vaccination series for subjects from parent trial DEN-315 (Mexico).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported