# Clinical trial results:
# An Open Label, Phase 2 Study to Investigate Cell-mediated Immunity and Safety of a Tetravalent Dengue Vaccine Candidate (TDV) Administered Subcutaneously in Healthy Children Aged 4 to 16 Years

## Summary

| | |
|---|---|
| EudraCT number | 2022-003456-13 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 13 December 2020 |

### Results information

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 26 January 2023 |
| First version publication date | 26 January 2023 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | DEN-313 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02948829 |
| WHO universal trial number (UTN) | U1111-1184-1893 |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Takeda |
| Sponsor organisation address | 95 Hayden Avenue, Lexington, United States, MA 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 | 13 December 2020 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 13 December 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to assess the cellular immune responses following 2 doses given 3 months apart of tetravalent dengue vaccine candidate (TDV) in 4 to 16 years' healthy participants.

Protection of trial subjects:

Study participants signed an Informed Consent Form. Assent is also obtained from the study participant where required.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 03 April 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Panama: 100 |
| Country: Number of subjects enrolled | Philippines: 100 |
| Worldwide total number of subjects | 200 |
| 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) | 190 |
| Adolescents (12-17 years) | 10 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at 2 investigative sites in Panama and Philippines from 03 April 2017 to 14 December 2020.

### Pre-assignment

Screening details:

Healthy participants were enrolled in a single arm in this study to receive 2 doses of Tetravalent Dengue Vaccine (TDV) injection subcutaneously (SC).

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | Tetravalent Dengue Vaccine (TDV) 0.5 mL |

Arm description:

TDV 0.5 mL, subcutaneous (SC) injection, on Day 1 (Month 0) and Day 90 (Month 3).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tetravalent Dengue Vaccine (TDV) 0.5 mL |
| Investigational medicinal product code | TAK-003 |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

TDV SC injection.

| **Number of subjects in period 1** | Tetravalent Dengue Vaccine (TDV) 0.5 mL |
|---|---|
| Started | 200 |
| Completed | 184 |
| Not completed | 16 |
| Other | 8 |
| Pregnancy | 1 |
| Withdrawal by Subject | 5 |
| Lost to follow-up | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Tetravalent Dengue Vaccine (TDV) 0.5 mL |
| Reporting group description: | |
| TDV 0.5 mL, subcutaneous (SC) injection, on Day 1 (Month 0) and Day 90 (Month 3). | |

| Reporting group values | Tetravalent Dengue Vaccine (TDV) 0.5 mL | Total | |
|---|---|---|---|
| Number of subjects | 200 | 200 | |
| Age Categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 6.7 | | |
| standard deviation | ± 2.28 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Male | 99 | 99 | |
| Female | 101 | 101 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 99 | 99 | |
| Not Hispanic or Latino | 101 | 101 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 76 | 76 | |
| Asian | 100 | 100 | |
| Black or African American | 8 | 8 | |
| White | 9 | 9 | |
| More than one race | 7 | 7 | |
| Baseline Seropositivity Status | | | |
| Seropositive at Baseline was defined as a reciprocal neutralizing titer >=10 for one or more dengue serotypes. Seronegative at Baseline was defined as having a reciprocal neutralizing titer <10 for all dengue serotypes. The 4 dengue virus serotypes were dengue virus (DENV)-1, DENV-2, DENV-3 and DENV-4. | | | |
| Units: Subjects | | | |
| Seropositive | 113 | 113 | |
| Seronegative | 87 | 87 | |
| Height | | | |
| Units: Cm | | | |
| arithmetic mean | 118.38 | | |
| standard deviation | ± 14.564 | - | |
| Weight | | | |
| Units: Kg | | | |
| arithmetic mean | 23.54 | | |
| standard deviation | ± 10.258 | - | |
| Body Mass Index (BMI) | | | |

| BMI = weight (kg)/[height (m)^2] | | | |
|---|---|---|---|
| Units: Kg/m^2 | | | |
| arithmetic mean | 16.15 | | |
| standard deviation | ± 3.104 | - | |

## Subject analysis sets

| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Panama |
|---|---|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Panama. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Philippines |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Philippines. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seropositive |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seropositive at Baseline. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seronegative |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seronegative status at Baseline. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: CD4+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): CD4+ T cells. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: CD8+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): CD8+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Panama: CD4+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Panama, CD4+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Philippines: CD4+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Philippines, CD4+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Panama: CD8+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Panama, CD8+ T cells. | |
| Subject analysis set title | TDV 0.5 ml: Philippines: CD8+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Philippines, CD8+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Seropositive: CD4+ T-Cells |

| | |
|---|---|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seropositive at Baseline, CD4+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Seronegative: CD4+ T-Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seronegative at Baseline, CD4+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Seropositive: CD8+ T- Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seropositive at Baseline, CD8+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Seronegative: CD8+ T-Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seronegative at Baseline, CD8+ T cells. | |

| **Reporting group values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Panama | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Philippines | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seropositive |
|---|---|---|---|
| Number of subjects | 97 | 98 | 109 |
| Age Categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Gender categorical<br>Units: Subjects | | | |
| Male<br>Female | | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino<br>Not Hispanic or Latino | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Black or African American<br>White<br>More than one race | | | |
| Baseline Seropositivity Status | | | |
| Seropositive at Baseline was defined as a reciprocal neutralizing titer >=10 for one or more dengue serotypes. Seronegative at Baseline was defined as having a reciprocal neutralizing titer <10 for all dengue serotypes. The 4 dengue virus serotypes were dengue virus (DENV)-1, DENV-2, DENV-3 and DENV-4. | | | |
| Units: Subjects | | | |
| Seropositive<br>Seronegative | | | |

| | | | |
|---|---|---|---|
| Height<br>Units: Cm<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Weight<br>Units: Kg<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Body Mass Index (BMI) | | | |
| BMI = weight (kg)/[height (m)^2] | | | |
| Units: Kg/m^2<br>arithmetic mean<br>standard deviation | ± | ± | ± |

| **Reporting group values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seronegative | Tetravalent Dengue Vaccine (TDV) 0.5 mL: CD4+ T Cells | Tetravalent Dengue Vaccine (TDV) 0.5 mL: CD8+ T Cells |
|---|---|---|---|
| Number of subjects | 86 | 79 | 79 |
| Age Categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Gender categorical<br>Units: Subjects | | | |
| Male<br>Female | | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino<br>Not Hispanic or Latino | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Black or African American<br>White<br>More than one race | | | |
| Baseline Seropositivity Status | | | |
| Seropositive at Baseline was defined as a reciprocal neutralizing titer >=10 for one or more dengue serotypes. Seronegative at Baseline was defined as having a reciprocal neutralizing titer <10 for all dengue serotypes. The 4 dengue virus serotypes were dengue virus (DENV)-1, DENV-2, DENV-3 and DENV-4. | | | |
| Units: Subjects | | | |
| Seropositive<br>Seronegative | | | |
| Height<br>Units: Cm<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Weight | | | |

| | | | |
|---|---|---|---|
| Units: Kg<br>arithmetic mean<br>standard deviation | ±<br> | ±<br> | ±<br> |
| Body Mass Index (BMI) | | | |
| BMI = weight (kg)/[height (m)^2] | | | |
| Units: Kg/m^2<br>arithmetic mean<br>standard deviation | ±<br> | ±<br> | ±<br> |

| **Reporting group values** | TDV 0.5 mL: Panama: CD4+ T Cells | TDV 0.5 mL: Philippines: CD4+ T Cells | TDV 0.5 mL: Panama: CD8+ T Cells |
|---|---|---|---|
| Number of subjects | 33 | 46 | 33 |
| Age Categorical<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | ±<br> | ±<br> | ±<br> |
| Gender categorical<br>Units: Subjects | | | |
| Male<br>Female | | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino<br>Not Hispanic or Latino | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Black or African American<br>White<br>More than one race | | | |
| Baseline Seropositivity Status | | | |
| Seropositive at Baseline was defined as a reciprocal neutralizing titer >=10 for one or more dengue serotypes. Seronegative at Baseline was defined as having a reciprocal neutralizing titer <10 for all dengue serotypes. The 4 dengue virus serotypes were dengue virus (DENV)-1, DENV-2, DENV-3 and DENV-4. | | | |
| Units: Subjects | | | |
| Seropositive<br>Seronegative | | | |
| Height<br>Units: Cm<br>arithmetic mean<br>standard deviation | ±<br> | ±<br> | ±<br> |
| Weight<br>Units: Kg<br>arithmetic mean<br>standard deviation | ±<br> | ±<br> | ±<br> |
| Body Mass Index (BMI) | | | |
| BMI = weight (kg)/[height (m)^2] | | | |

| | | | |
|---|---|---|---|
| Units: Kg/m^2 | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | ± |

| **Reporting group values** | TDV 0.5 ml: Philippines: CD8+ T Cells | TDV 0.5 mL: Seropositive: CD4+ T-Cells | TDV 0.5 mL: Seronegative: CD4+ T-Cells |
|---|---|---|---|
| Number of subjects | 46 | 44 | 35 |
| Age Categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | 0 | 0 |
| standard deviation | ± | ± | ± |
| Gender categorical | | | |
| Units: Subjects | | | |
| Male | | 0 | 0 |
| Female | | 0 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | | 0 | 0 |
| Not Hispanic or Latino | | 0 | 0 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | | 0 | 0 |
| Asian | | 0 | 0 |
| Black or African American | | 0 | 0 |
| White | | 0 | 0 |
| More than one race | | 0 | 0 |
| Baseline Seropositivity Status | | | |
| Seropositive at Baseline was defined as a reciprocal neutralizing titer >=10 for one or more dengue serotypes. Seronegative at Baseline was defined as having a reciprocal neutralizing titer <10 for all dengue serotypes. The 4 dengue virus serotypes were dengue virus (DENV)-1, DENV-2, DENV-3 and DENV-4. | | | |
| Units: Subjects | | | |
| Seropositive | | 0 | 0 |
| Seronegative | | 0 | 0 |
| Height | | | |
| Units: Cm | | | |
| arithmetic mean | | 0 | 0 |
| standard deviation | ± | ± | ± |
| Weight | | | |
| Units: Kg | | | |
| arithmetic mean | | 0 | 0 |
| standard deviation | ± | ± | ± |
| Body Mass Index (BMI) | | | |
| BMI = weight (kg)/[height (m)^2] | | | |
| Units: Kg/m^2 | | | |
| arithmetic mean | | 0 | 0 |
| standard deviation | ± | ± | ± |

| **Reporting group values** | TDV 0.5 mL: | TDV 0.5 mL: | |
|---|---|---|---|

| | Seropositive: CD8+ T- Cells | Seronegative: CD8+ T-Cells | |
|---|---|---|---|
| Number of subjects | 44 | 35 | |
| Age Categorical<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age continuous<br>Units: years | | | |
| arithmetic mean | 0 | 0 | |
| standard deviation | ± | ± | |
| Gender categorical<br>Units: Subjects | | | |
| Male | 0 | 0 | |
| Female | 0 | 0 | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 0 | 0 | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 0 | 0 | |
| More than one race | 0 | 0 | |
| Baseline Seropositivity Status | | | |
| Seropositive at Baseline was defined as a reciprocal neutralizing titer >=10 for one or more dengue serotypes. Seronegative at Baseline was defined as having a reciprocal neutralizing titer <10 for all dengue serotypes. The 4 dengue virus serotypes were dengue virus (DENV)-1, DENV-2, DENV-3 and DENV-4. | | | |
| Units: Subjects | | | |
| Seropositive | 0 | 0 | |
| Seronegative | 0 | 0 | |
| Height<br>Units: Cm | | | |
| arithmetic mean | 0 | 0 | |
| standard deviation | ± | ± | |
| Weight<br>Units: Kg | | | |
| arithmetic mean | 0 | 0 | |
| standard deviation | ± | ± | |
| Body Mass Index (BMI) | | | |
| BMI = weight (kg)/[height (m)^2] | | | |
| Units: Kg/m^2 | | | |
| arithmetic mean | 0 | 0 | |
| standard deviation | ± | ± | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Tetravalent Dengue Vaccine (TDV) 0.5 mL |
| Reporting group description: TDV 0.5 mL, subcutaneous (SC) injection, on Day 1 (Month 0) and Day 90 (Month 3). | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Panama |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Panama. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Philippines |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Philippines. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seropositive |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seropositive at Baseline. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seronegative |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seronegative status at Baseline. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: CD4+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): CD4+ T cells. | |
| Subject analysis set title | Tetravalent Dengue Vaccine (TDV) 0.5 mL: CD8+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): CD8+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Panama: CD4+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Panama, CD4+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Philippines: CD4+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Philippines, CD4+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Panama: CD8+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Panama, CD8+ T cells. | |
| Subject analysis set title | TDV 0.5 ml: Philippines: CD8+ T Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants from Philippines, CD8+ T cells. | |

| | |
|---|---|
| Subject analysis set title | TDV 0.5 mL: Seropositive: CD4+ T-Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seropositive at Baseline, CD4+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Seronegative: CD4+ T-Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seronegative at Baseline, CD4+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Seropositive: CD8+ T- Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seropositive at Baseline, CD8+ T cells. | |
| Subject analysis set title | TDV 0.5 mL: Seronegative: CD8+ T-Cells |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: TDV 0.5 mL, SC injection, on Day 1 (Month 0) and Day 90 (Month 3): Participants seronegative at Baseline, CD8+ T cells. | |

## Primary: Percentage of Participants With Cellular Immune Response to 2 Doses of Tetravalent Dengue Vaccine (TDV) at 1 Month Post Second Vaccination

| | |
|---|---|
| End point title | Percentage of Participants With Cellular Immune Response to 2 Doses of Tetravalent Dengue Vaccine (TDV) at 1 Month Post Second Vaccination[1] |
| End point description: Percentage of participants with cellular immune response were reported. Cellular immune response was defined as an interferon-gamma (IFN-γ) enzyme-linked immunospot (ELISPOT) response that was >3 times higher compared to Baseline (Day 1) and ≥ 5 spots per well. Cellular immune response to any peptide pool was reported. The peptide pool included non-structural protein (NS) for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. Per-Protocol Set (PPS) included all participants from the Full Analysis Set (FAS) who have no major protocol violations. Overall number of participants analysed are participants with data available for analysis. | |
| End point type | Primary |
| End point timeframe: 1 month post second vaccination (Day 120) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for this outcome measure.

| End point values | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 173 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 86.1 (80.1 to 90.9) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Magnitude of Cellular Immune Response Assessed by Number of Spot Forming Cells (SFC)/Million Peripheral Blood Mononuclear Cells (PBMCs) Measured by IFN-γ ELISPOT at 1 Month Post Second Vaccination

| End point title | Magnitude of Cellular Immune Response Assessed by Number of Spot Forming Cells (SFC)/Million Peripheral Blood Mononuclear Cells (PBMCs) Measured by IFN-γ ELISPOT at 1 Month Post Second Vaccination |
|---|---|

End point description:

The magnitude of cellular immune response was assessed by the number of SFC/million PBMCs for participants with a cellular immune response. Cellular immune response was defined as IFN-γ ELISPOT response that was >3 times higher compared to Baseline (Day 1) and ≥ 5 spots per well. Data (SFC/million PBMC) for participants with a cellular immune response to any peptide pool is reported. The peptide pool included NS for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. PPS included all participants from the FAS who have no major protocol violations. Overall number of participants analysed are participants with data available for analysis.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post second vaccination (Day 120)

| **End point values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 149 | | | |
| Units: SFC/million PBMCs | | | | |
| median (inter-quartile range (Q1-Q3)) | 1003.0 (443.0 to 2126.0) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Cellular Immune Response to TDV at 1 Month Post First Vaccination and 6 Months Post Second Vaccination

| End point title | Percentage of Participants With Cellular Immune Response to TDV at 1 Month Post First Vaccination and 6 Months Post Second Vaccination |
|---|---|

End point description:

Percentage of participants with cellular immune response were reported. Cellular immune response was defined as an IFN-γ ELISPOT response that was >3 times higher compared to Baseline (Day 1 [M0]) and >=5 spots per well. Cellular immune response to any peptide pool was reported. The peptide pool included NS for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. PPS included all participants from the FAS who have no major protocol violations. Number analysed is the number of participants with data available for analysis at the given timepoint.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); 6 month post second vaccination (Day 270)

| End point values | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Day 30 | 86.0 (79.8 to 90.8) | | | |
| Day 270 | 86.7 (80.7 to 91.4) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Magnitude of Cellular Immune Response Assessed by Number of SFC/Million PBMCs Measured by IFN-γ ELISPOT at 1 Month Post First Vaccination and 6 Months Post Second Vaccination

| End point title | Magnitude of Cellular Immune Response Assessed by Number of SFC/Million PBMCs Measured by IFN-γ ELISPOT at 1 Month Post First Vaccination and 6 Months Post Second Vaccination |
|---|---|

End point description:

The magnitude of cellular immune response was assessed by the number of SFC/million PBMCs for participants with a cellular immune response. Cellular immune response was defined as IFN-γ ELISPOT response that was >3 times higher compared to Baseline (Day 1) and ≥ 5 spots per well. Data (SFC/million PBMC) for participants with a cellular immune response to any peptide pool is reported. The peptide pool included NS protein for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. PPS included all participants from the FAS who have no major protocol violations. Number analysed is the number of participants with data available for analysis at the given timepoint.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); 6 month post second vaccination (Day 270)

| End point values | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195 | | | |
| Units: SFC/million PBMCs | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Day 30 | 1181.0 (585.0 to 2891.0) | | | |
| Day 270 | 572.5 (250.0 to 1382.0) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Cellular Immune Responses to TDV at 1 Month Post First Vaccination, 1 and 6 Months Post Second Vaccination Post Second Vaccination Assessed by Country

| End point title | Percentage of Participants With Cellular Immune Responses to TDV at 1 Month Post First Vaccination, 1 and 6 Months Post Second Vaccination Post Second Vaccination Assessed by Country |
|---|---|

End point description:

Percentage of participants with cellular immune response by country (Panama and Philippines) were reported. Cellular immune response was defined as an IFN-γ ELISPOT response that was >3 times higher compared to Baseline (Day 1 [M0]) and >=5 spots per well. Cellular immune response to any peptide pool was reported. The peptide pool included NS for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. PPS 'by country' included all participants from the FAS who have no major protocol violations. Number analysed is the number of participants with data available for analysis at the given timepoint.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); 1 and 6 months post second vaccination (Days 120 Days 270)

| **End point values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Panama | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Philippines | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 97 | 98 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Day 30 | 88.2 (78.7 to 94.4) | 84.2 (75.3 to 90.9) | | |
| Day 120 | 84.0 (73.7 to 91.4) | 87.8 (79.6 to 93.5) | | |
| Day 270 | 90.7 (81.7 to 96.2) | 83.7 (74.8 to 90.4) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Cellular Immune Responses to TDV:1 Month Post First Vaccination, 1 and 6 Months Post Second Vaccination Post Second

## Vaccination, by Dengue Baseline Seropositivity Status

| End point title | Percentage of Participants With Cellular Immune Responses to TDV:1 Month Post First Vaccination, 1 and 6 Months Post Second Vaccination Post Second Vaccination, by Dengue Baseline Seropositivity Status |
|---|---|

End point description:

Percentage of participants with cellular immune response by dengue Baseline seropositivity status (Seropositive and Seronegative) were reported. Cellular immune response was defined as an IFN-γ ELISPOT response that was >3 times higher compared to Baseline (Day 1 [M0]) and >=5 spots per well. Seropositive at Baseline was defined as a reciprocal neutralizing titer >=10 for one or more dengue serotypes. Seronegative at Baseline was defined as having a reciprocal neutralizing titer <10 for all dengue serotypes. The 4 dengue virus serotypes were dengue virus (DENV)-1, DENV-2, DENV-3 and DENV-4. Cellular immune response to any peptide pool was reported. The peptide pool included NS for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. PPS 'by Baseline seropositivity status' included all participants from the FAS who have no major protocol violations. Number analysed is the number of participants with data available for analysis at the given timepoint.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); 1 and 6 months post second vaccination (Days 120 Days 270)

| **End point values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seropositive | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seronegative | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 109 | 86 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Day 30 | 81.4 (72.3 to 88.6) | 91.9 (83.2 to 97.0) | | |
| Day 120 | 82.0 (73.1 to 89.0) | 91.8 (83.0 to 96.9) | | |
| Day 270 | 80.2 (71.1 to 87.5) | 95.8 (88.3 to 99.1) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Magnitude of Cellular Immune Response Assessed by Number of SFC/Million PBMCs Measured by IFN-γ ELISPOT at 1 Month Post First, 1 and 6 Months Post Second Vaccination, by Country

| End point title | Magnitude of Cellular Immune Response Assessed by Number of SFC/Million PBMCs Measured by IFN-γ ELISPOT at 1 Month Post First, 1 and 6 Months Post Second Vaccination, by Country |
|---|---|

End point description:

The magnitude of cellular immune response by country (Panama and Philippines) was assessed by the number of SFC/million PBMCs for participants with a cellular immune response. Cellular immune response was defined as IFN-γ ELISPOT response that was >3 times higher compared to Baseline (Day 1) and ≥ 5 spots per well. Data (SFC/million PBMC) for participants with a cellular immune response to any peptide pool is reported. The peptide pool included NS protein for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. PPS 'by country' included all participants from the FAS who have no major protocol violations. Number analysed is the number of participants with data available at the

given timepoint.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); 1and 6 months post second vaccination (Days 120 Days 270)

| **End point values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Panama | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Philippines | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 97 | 98 | | |
| Units: SFC/million PBMCs | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Day 30 | 1091.0 (533.0 to 2988.0) | 1268.5 (672.5 to 2797.0) | | |
| Day 120 | 919.0 (360.0 to 1679.0) | 1086.0 (513.0 to 2304.0) | | |
| Day 270 | 439.0 (215.5 to 1428.5) | 612.0 (263.0 to 1264.0) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Magnitude of Cellular Immune Response Assessed by Number of SFC/Million PBMCs Measured by IFN-γ ELISPOT 1 Month Post First; 1 and 6 Months Post Second Vaccination, by Dengue Baseline Seropositivity Status

| End point title | Magnitude of Cellular Immune Response Assessed by Number of SFC/Million PBMCs Measured by IFN-γ ELISPOT 1 Month Post First; 1 and 6 Months Post Second Vaccination, by Dengue Baseline Seropositivity Status |
|---|---|

End point description:

The magnitude of cellular immune response by dengue Baseline seropositivity status (Seropositive and Seronegative) was assessed by the number of SFC/million PBMCs for participants with a cellular immune response. Cellular immune response:IFN-γ ELISPOT response that was >3 times higher compared to Baseline (Day 1) and ≥ 5 spots per well. Seropositive at Baseline:a reciprocal neutralizing titer >=10 for one or more dengue serotypes. Seronegative at Baseline:having a reciprocal neutralizing titer <10 for all dengue serotypes. The 4 dengue virus serotypes were dengue virus (DENV)-1, DENV-2, DENV-3 and DENV-4. Cellular immune response to any peptide pool was reported. The peptide pool included NS for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. PPS 'by Baseline seropositivity status' included all participants from the FAS who have no major protocol violations. Number analysed:number of participants with data available for analysis at the given timepoint.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); 1and 6 months post second vaccination (Days 120 Days 270)

| End point values | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seropositive | Tetravalent Dengue Vaccine (TDV) 0.5 mL: Seronegative | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 109 | 86 | | |
| Units: SFC/million PBMCs | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Day 30 | 1735.0 (736.0 to 3461.0) | 894.0 (527.0 to 2011.0) | | |
| Day 120 | 1216.0 (584.0 to 2774.0) | 743.0 (377.0 to 1546.0) | | |
| Day 270 | 719.0 (287.0 to 1684.0) | 416.0 (245.0 to 808.0) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Cellular Immune Response to TDV in Participants >10 Years of Age

| End point title | Percentage of Participants With Cellular Immune Response to TDV in Participants >10 Years of Age |
|---|---|

End point description:

Percentage of participants with cellular immune response in participants >10 years of age were reported. Cellular immune response was defined as an IFN-γ ELISPOT response that was >3 times higher compared to Baseline (Day 1 [M0]) and >=5 spots per well. Cellular immune response to any peptide pool was reported. The peptide pool included NS for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. SFC/million PBMC for any peptide pool is reported in participants >10 years of age. The analysis of samples collected at Day 90 and annually at Years 1, 2 and 3 for outcome measures related to assessment of the cellular immune response is still ongoing because of the limited testing capacities of the laboratory due to COVID-19; the data will be reported when available.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 14

| End point values | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[2] | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |

Notes:

[2] - Data for this outcome measure was not analysed as planned due to testing incapacities of laboratory.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Magnitude of Cellular Immune Response Assessed by Number of SFC/Million PBMCs Measured by IFN-γ ELISPOT in Participants >10 Years of Age

| End point title | Magnitude of Cellular Immune Response Assessed by Number of SFC/Million PBMCs Measured by IFN-γ ELISPOT in Participants >10 Years of Age |
|---|---|

End point description:

The magnitude of cellular immune response was assessed by the number of SFC/million PBMCs for participants with a cellular immune response. Cellular immune response was defined as IFN-γ ELISPOT response that was >3 times higher compared to Baseline (Day 1) and ≥ 5 spots per well. Cellular immune response to any peptide pool was reported. The peptide pool included NS for each of the dengue serotype: DENV-1, DENV-2, DENV-3 and DENV-4. SFC/million PBMC for any peptide pool is reported in participants >10 years of age. The analysis of samples collected at Day 90 and annually at Years 1, 2 and 3 for outcome measures related to assessment of the cellular immune response is still ongoing because of the limited testing capacities of the laboratory due to COVID-19; the data will be reported when available.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 14

| **End point values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[3] | | | |
| Units: SFC/million PBMC | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |

Notes:

[3] - Data for this outcome measure was not analysed as planned due to testing incapacities of laboratory.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Phenotype Characterization of Cellular Immune Response Assessed by Percentage of Total T Cells of Cellular Response to DENV-2 NS Proteins at 1 Month Post First, 1 and 6 Months Post Second Vaccination

| End point title | Phenotype Characterization of Cellular Immune Response Assessed by Percentage of Total T Cells of Cellular Response to DENV-2 NS Proteins at 1 Month Post First, 1 and 6 Months Post Second Vaccination |
|---|---|

End point description:

The phenotype characterization of cellular immune response was assessed by intracellular cytokine staining (ICS) by the frequency of total cluster of differentiation 4 (CD4)+ and CD8+ T cells and was performed in a subset of participants with IFN- γ ELISPOT responses >500 SFC/million cells and availability of sufficient cells. The peptide pools included NS for the DENV-2 serotype. Data are presented for the different expression profiles of interferon-gamma (IFN-γ), interleukin-2 (IL-2) and tumor necrosis factor-alpha (TNF-α) cytokines for each peptide pool. Data is reported based on the type of T cells present in participants at the time of analysis (CD4+ T cells and CD8+ T cells). ICS Subset 'by T-cells' included participants from PPS who have IFN-γ ELISPOT responses >500 SFC/million PBMCs and availability of sufficient cells. Number analysed is the number of participants with data available for analysis for specific category.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); 1and 6 months post second vaccination (Days 120 Days 270)

| End point values | Tetravalent Dengue Vaccine (TDV) 0.5 mL: CD4+ T Cells | Tetravalent Dengue Vaccine (TDV) 0.5 mL: CD8+ T Cells | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 79 | 79 | | |
| Units: percentage of T cells | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IFNg+IL2+TNFa+, DENV-2, NS1-2, Day 30 | 0.008980 (0.003840 to 0.020000) | 0.001470 (0.000000 to 0.008470) | | |
| IFNg+IL2+TNFa+, DENV-2, NS3-2, Day 30 | 0.005140 (0.001980 to 0.010000) | 0.020000 (0.003400 to 0.039350) | | |
| IFNg+IL2+TNFa+, DENV-2, NS5-2, Day 30 | 0.005380 (0.002890 to 0.011000) | 0.016000 (0.003190 to 0.049000) | | |
| IFNg+IL2+TNFa-, DENV-2, NS1-2, Day 30 | 0.000000 (0.000000 to 0.001170) | 0.000000 (0.000000 to 0.000000) | | |
| IFNg+IL2+TNFa-, DENV-2, NS3-2, Day 30 | 0.000000 (0.000000 to 0.000000) | 0.001210 (0.000000 to 0.002980) | | |
| IFNg+IL2+TNFa-, DENV-2, NS5-2, Day 30 | 0.000000 (0.000000 to 0.000000) | 0.001610 (0.000000 to 0.004370) | | |
| IFNg+IL2-TNFa+, DENV-2, NS1-2, Day 30 | 0.004210 (0.000580 to 0.006770) | 0.018180 (0.000190 to 0.054000) | | |
| IFNg+IL2-TNFa+, DENV-2, NS3-2, Day 30 | 0.002950 (0.000420 to 0.006480) | 0.164350 (0.058000 to 0.448100) | | |
| IFNg+IL2-TNFa+, DENV-2, NS5-2, Day 30 | 0.003460 (0.000070 to 0.006280) | 0.145490 (0.034000 to 0.390000) | | |
| IFNg-IL2+TNFa+, DENV-2, NS1-2, Day 30 | 0.002480 (0.000000 to 0.007470) | 0.000000 (0.000000 to 0.000000) | | |
| IFNg-IL2+TNFa+, DENV-2, NS3-2, Day 30 | 0.002000 (0.000000 to 0.007290) | 0.000000 (0.000000 to 0.000310) | | |
| IFNg-IL2+TNFa+, DENV-2, NS5-2, Day 30 | 0.003350 (0.000000 to 0.008000) | 0.000000 (0.000000 to 0.000000) | | |
| IFNg+IL2-TNFa-, DENV-2, NS1-2, Day 30 | 0.000570 (0.000000 to 0.004590) | 0.007250 (0.002000 to 0.028000) | | |
| IFNg+IL2-TNFa-, DENV-2, NS3-2, Day 30 | 0.000130 (0.000000 to 0.003030) | 0.053000 (0.024540 to 0.208580) | | |
| IFNg+IL2-TNFa-, DENV-2, NS5-2, Day 30 | 0.000740 (0.000000 to 0.003520) | 0.063490 (0.017000 to 0.215820) | | |
| IFNg-IL2+TNFa-, DENV-2, NS1-2, Day 30 | 0.001000 (0.000000 to 0.009000) | 0.002000 (0.000000 to 0.009000) | | |

| | | | | |
|---|---|---|---|---|
| IFNg-IL2+TNFa-, DENV-2, NS3-2, Day 30 | 0.000000 (0.000000 to 0.007000) | 0.000000 (0.000000 to 0.008220) | | |
| IFNg-IL2+TNFa-, DENV-2, NS5-2, Day 30 | 0.000000 (0.000000 to 0.009000) | 0.002000 (0.000000 to 0.010000) | | |
| IFNg-IL2-TNFa+, DENV-2, NS1-2, Day 30 | 0.000000 (0.000000 to 0.028000) | 0.000000 (0.000000 to 0.013000) | | |
| IFNg-IL2-TNFa+, DENV-2, NS3-2, Day 30 | 0.010000 (0.000000 to 0.040000) | 0.012000 (0.000000 to 0.030000) | | |
| IFNg-IL2-TNFa+, DENV-2, NS5-2, Day 30 | 0.010000 (0.000000 to 0.050000) | 0.010000 (0.000000 to 0.030000) | | |
| IFNg+IL2+TNFa+, DENV-2, NS1-2, Day 120 | 0.008340 (0.003340 to 0.017000) | 0.001320 (0.000000 to 0.004240) | | |
| IFNg+IL2+TNFa+, DENV-2, NS3-2, Day 120 | 0.003410 (0.001041 to 0.007190) | 0.010000 (0.002650 to 0.018000) | | |
| IFNg+IL2+TNFa+, DENV-2, NS5-2, Day 120 | 0.002100 (0.000000 to 0.004710) | 0.007850 (0.002230 to 0.027000) | | |
| IFNg+IL2+TNFa-, DENV-2, NS1-2, Day 120 | 0.001050 (0.000000 to 0.002420) | 0.000000 (0.000000 to 0.000000) | | |
| IFNg+IL2+TNFa-, DENV-2, NS3-2, Day 120 | 0.000000 (0.000000 to 0.001420) | 0.000000 (0.000000 to 0.001800) | | |
| IFNg+IL2+TNFa-, DENV-2, NS5-2, Day 120 | 0.000000 (0.000000 to 0.000935) | 0.000960 (0.000000 to 0.002340) | | |
| IFNg+IL2-TNFa+, DENV-2, NS1-2, Day 120 | 0.002110 (0.000000 to 0.005070) | 0.007340 (0.000000 to 0.029850) | | |
| IFNg+IL2-TNFa+, DENV-2, NS3-2, Day 120 | 0.002000 (0.000000 to 0.004160) | 0.116110 (0.047000 to 0.317000) | | |
| IFNg+IL2-TNFa+, DENV-2, NS5-2, Day 120 | 0.000860 (0.000000 to 0.002820) | 0.096230 (0.030050 to 0.207090) | | |
| IFNg-IL2+TNFa+, DENV-2, NS1-2, Day 120 | 0.007160 (0.002000 to 0.015040) | 0.000000 (0.000000 to 0.000000) | | |
| IFNg-IL2+TNFa+, DENV-2, NS3-2, Day 120 | 0.000000 (0.000000 to 0.004710) | 0.000000 (0.000000 to 0.000000) | | |
| IFNg-IL2+TNFa+, DENV-2, NS5-2, Day 120 | 0.003350 (0.000000 to 0.009000) | 0.000000 (0.000000 to 0.001250) | | |
| IFNg+IL2-TNFa-, DENV-2, NS1-2, Day 120 | 0.002070 (0.000000 to 0.005030) | 0.004080 (0.000000 to 0.011000) | | |
| IFNg+IL2-TNFa-, DENV-2, NS3-2, Day 120 | 0.000990 (0.000000 to 0.002630) | 0.038000 (0.013270 to 0.094810) | | |
| IFNg+IL2-TNFa-, DENV-2, NS5-2, Day 120 | 0.000000 (0.000000 to 0.002480) | 0.018850 (0.007000 to 0.060560) | | |
| IFNg-IL2+TNFa-, DENV-2, NS1-2, Day 120 | 0.009000 (0.000000 to 0.014000) | 0.002000 (0.000000 to 0.014000) | | |

| | | | | |
|---|---|---|---|---|
| IFNg-IL2+TNFa-, DENV-2, NS3-2, Day 120 | 0.001000 (0.000000 to 0.010000) | 0.001000 (0.000000 to 0.017000) | | |
| IFNg-IL2+TNFa-, DENV-2, NS5-2, Day 120 | 0.000000 (0.000000 to 0.013000) | 0.001000 (0.000000 to 0.015000) | | |
| IFNg-IL2-TNFa+, DENV-2, NS1-2, Day 120 | 0.002000 (0.000000 to 0.028000) | 0.004000 (0.000000 to 0.020000) | | |
| IFNg+IL2+TNFa-, DENV-2, NS3-2, Day 270 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001505) | | |
| IFNg+IL2+TNFa-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001485) | | |
| IFNg+IL2-TNFa+, DENV-2, NS1-2, Day 270 | 0.001052 (0.000000 to 0.003300) | 0.005185 (0.000030 to 0.023975) | | |
| IFNg+IL2-TNFa+, DENV-2, NS3-2, Day 270 | 0.001500 (0.000000 to 0.003455) | 0.092000 (0.034045 to 0.264215) | | |
| IFNg+IL2-TNFa+, DENV-2, NS5-2, Day 270 | 0.000185 (0.000000 to 0.002785) | 0.069500 (0.022135 to 0.204995) | | |
| IFNg-IL2+TNFa+, DENV-2, NS1-2, Day 270 | 0.005065 (0.001000 to 0.010945) | 0.000000 (0.000000 to 0.000000) | | |
| IFNg-IL2+TNFa+, DENV-2, NS3-2, Day 270 | 0.001175 (0.000000 to 0.005160) | 0.000000 (0.000000 to 0.000000) | | |
| IFNg-IL2+TNFa+, DENV-2, NS5-2, Day 270 | 0.001670 (0.000000 to 0.005240) | 0.000000 (0.000000 to 0.000000) | | |
| IFNg+IL2-TNFa-, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.002675) | 0.003665 (0.000000 to 0.008825) | | |
| IFNg+IL2-TNFa-, DENV-2, NS3-2, Day 270 | 0.000000 (0.000000 to 0.001870) | 0.015325 (0.002385 to 0.030105) | | |
| IFNg+IL2-TNFa-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.002565) | 0.012000 (0.000530 to 0.028580) | | |
| IFNg-IL2+TNFa-, DENV-2, NS1-2, Day 270 | 0.000500 (0.000000 to 0.008500) | 0.001000 (0.000000 to 0.006500) | | |
| IFNg-IL2+TNFa-, DENV-2, NS3-2, Day 270 | 0.000000 (0.000000 to 0.001000) | 0.000000 (0.000000 to 0.003730) | | |
| IFNg-IL2+TNFa-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.006000) | 0.000000 (0.000000 to 0.006500) | | |
| IFNg-IL2-TNFa+-, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.019000) | 0.004500 (0.000000 to 0.020000) | | |
| IFNg-IL2-TNFa+-, DENV-2, NS3-2, Day 270 | 0.008000 (0.000000 to 0.030000) | 0.015500 (0.000000 to 0.045500) | | |
| IFNg-IL2-TNFa+-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.040000) | 0.016500 (0.000000 to 0.037000) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phenotype Characterization of Cellular Immune Response Assessed by Percentage of Total T Cells of Cellular Response DENV-2 NS Proteins,1 Month Post First;1 and 6 Months Post Second Vaccination, by Country

| End point title | Phenotype Characterization of Cellular Immune Response Assessed by Percentage of Total T Cells of Cellular Response DENV-2 NS Proteins,1 Month Post First;1 and 6 Months Post Second Vaccination, by Country |
|---|---|

End point description:

The phenotype characterization of cellular immune response by country was assessed by ICS by the frequency of total CD4+ and CD8+ T cells and was performed in a subset of participants with IFN- γ ELISPOT responses >500 SFC/million cells and availability of sufficient cells. The peptide pools included NS for the DENV-2 serotype. Data are presented for the different expression profiles of IFN-γ, IL-2 and TNF-α cytokines for each peptide pool. Data is reported per country (Panama and Philippines) based on the type of T cells present in participants at the time of analysis (CD4+ T cells and CD8+ T cells). ICS Subset 'by country based on T-cells' included participants from PPS who have IFN-γ ELISPOT responses >500 SFC/million PBMCs and availability of sufficient cells. Number analysed is the number of participants with data available for analysis for specific category.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); 1and 6 months post second vaccination (Days 120 Days 270)

| End point values | TDV 0.5 mL: Panama: CD4+ T Cells | TDV 0.5 mL: Philippines: CD4+ T Cells | TDV 0.5 mL: Panama: CD8+ T Cells | TDV 0.5 ml: Philippines: CD8+ T Cells |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 33 | 46 | 33 | 46 |
| Units: percentage of T cells | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IFNg+IL2+TNFa+, DENV-2, NS1-2, Day 30 | 0.006290 (0.001180 to 0.020000) | 0.010500 (0.005950 to 0.020500) | 0.002020 (0.000000 to 0.032000) | 0.001410 (0.000000 to 0.006160) |
| IFNg+IL2+TNFa+, DENV-2, NS3-2, Day 30 | 0.002780 (0.001700 to 0.006630) | 0.007780 (0.002095 to 0.012520) | 0.020000 (0.002210 to 0.036000) | 0.020500 (0.005265 to 0.040175) |
| IFNg+IL2+TNFa+, DENV-2, NS5-2, Day 30 | 0.003870 (0.002140 to 0.007600) | 0.005815 (0.003360 to 0.012000) | 0.025000 (0.003530 to 0.043000) | 0.014790 (0.003137 to 0.050000) |
| IFNg+IL2+TNFa-, DENV-2, NS1-2, Day 30 | 0.000000 (0.000000 to 0.001770) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2+TNFa-, DENV-2, NS3-2, Day 30 | 0.000000 (0.000000 to 0.000927) | 0.000000 (0.000000 to 0.000000) | 0.001330 (0.000000 to 0.003000) | 0.001080 (0.000000 to 0.002695) |
| IFNg+IL2+TNFa-, DENV-2, NS5-2, Day 30 | 0.000000 (0.000000 to 0.000373) | 0.000000 (0.000000 to 0.000000) | 0.001880 (0.000000 to 0.004370) | 0.001490 (0.000000 to 0.004960) |
| IFNg+IL2-TNFa+, DENV-2, NS1-2, Day 30 | 0.004270 (0.000000 to 0.006690) | 0.003965 (0.000660 to 0.009180) | 0.031000 (0.001060 to 0.164020) | 0.013450 (0.000095 to 0.030165) |
| IFNg+IL2-TNFa+, DENV-2, NS3-2, Day 30 | 0.002810 (0.000000 to 0.005090) | 0.003200 (0.000525 to 0.006710) | 0.134020 (0.039510 to 0.420000) | 0.179260 (0.064360 to 0.539560) |

| | | | | |
|---|---|---|---|---|
| IFNg+IL2-TNFa+, DENV-2, NS5-2, Day 30 | 0.003460 (0.000070 to 0.006000) | 0.003515 (0.000505 to 0.006655) | 0.150000 (0.062000 to 0.382000) | 0.144180 (0.024090 to 0.429000) |
| IFNg-IL2+TNFa+, DENV-2, NS1-2, Day 30 | 0.002070 (0.000000 to 0.005110) | 0.004246 (0.000000 to 0.010235) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa+, DENV-2, NS3-2, Day 30 | 0.002110 (0.000000 to 0.010630) | 0.001680 (0.000000 to 0.006350) | 0.000000 (0.000000 to 0.000760) | 0.000000 (0.000000 to 0.000090) |
| IFNg-IL2+TNFa+, DENV-2, NS5-2, Day 30 | 0.003000 (0.000000 to 0.009000) | 0.003390 (0.000000 to 0.007805) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2-TNFa-, DENV-2, NS1-2, Day 30 | 0.000490 (0.000000 to 0.005030) | 0.000710 (0.000000 to 0.003450) | 0.027540 (0.005000 to 0.062490) | 0.005115 (0.000820 to 0.013695) |
| IFNg+IL2-TNFa-, DENV-2, NS3-2, Day 30 | 0.001240 (0.000000 to 0.002890) | 0.000000 (0.000000 to 0.003210) | 0.060020 (0.025260 to 0.170000) | 0.050360 (0.022270 to 0.301000) |
| IFNg+IL2-TNFa-, DENV-2, NS5-2, Day 30 | 0.000620 (0.000000 to 0.002690) | 0.000825 (0.000000 to 0.003600) | 0.085000 (0.021000 to 0.166000) | 0.053260 (0.013595 to 0.226605) |
| IFNg-IL2+TNFa-, DENV-2, NS1-2, Day 30 | 0.005000 (0.000000 to 0.011290) | 0.000000 (0.000000 to 0.005000) | 0.003000 (0.000000 to 0.011000) | 0.001810 (0.000000 to 0.008000) |
| IFNg-IL2+TNFa-, DENV-2, NS3-2, Day 30 | 0.001000 (0.000000 to 0.012000) | 0.000000 (0.000000 to 0.002000) | 0.000000 (0.000000 to 0.009000) | 0.001000 (0.000000 to 0.006365) |
| IFNg-IL2+TNFa-, DENV-2, NS5-2, Day 30 | 0.006290 (0.000000 to 0.019000) | 0.000000 (0.000000 to 0.004000) | 0.007000 (0.000000 to 0.010000) | 0.000000 (0.000000 to 0.009000) |
| IFNg-IL2-TNFa+, DENV-2, NS1-2, Day 30 | 0.000000 (0.000000 to 0.009000) | 0.000000 (0.000000 to 0.035000) | 0.005000 (0.000000 to 0.021000) | 0.000000 (0.000000 to 0.010000) |
| IFNg-IL2-TNFa+, DENV-2, NS3-2, Day 30 | 0.008000 (0.000000 to 0.030000) | 0.010000 (0.000000 to 0.046000) | 0.009000 (0.003000 to 0.020000) | 0.013000 (0.000000 to 0.037500) |
| IFNg-IL2-TNFa+, DENV-2, NS5-2, Day 30 | 0.000000 (0.000000 to 0.040000) | 0.015000 (0.000000 to 0.055000) | 0.010000 (0.000000 to 0.027000) | 0.001000 (0.000000 to 0.034000) |
| IFNg+IL2+TNFa+, DENV-2, NS1-2, Day 120 | 0.005531 (0.003340 to 0.012780) | 0.009230 (0.003860 to 0.018610) | 0.001590 (0.000000 to 0.006910) | 0.001100 (0.000000 to 0.002580) |
| IFNg+IL2+TNFa+, DENV-2, NS3-2, Day 120 | 0.002690 (0.001041 to 0.007190) | 0.003495 (0.001420 to 0.006660) | 0.010000 (0.002850 to 0.016000) | 0.010000 (0.002650 to 0.019000) |
| IFNg+IL2+TNFa+, DENV-2, NS5-2, Day 120 | 0.000661 (0.000000 to 0.002990) | 0.002598 (0.000000 to 0.005470) | 0.013000 (0.004830 to 0.021000) | 0.006905 (0.001180 to 0.028000) |
| IFNg+IL2+TNFa-, DENV-2, NS1-2, Day 120 | 0.000900 (0.000000 to 0.002580) | 0.001135 (0.000000 to 0.002180) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2+TNFa-, DENV-2, NS3-2, Day 120 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001670) | 0.000000 (0.000000 to 0.001440) | 0.000000 (0.000000 to 0.001920) |
| IFNg+IL2+TNFa-, DENV-2, NS5-2, Day 120 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001190) | 0.000000 (0.000000 to 0.001650) | 0.001175 (0.000000 to 0.003450) |
| IFNg+IL2-TNFa+, DENV-2, NS1-2, Day 120 | 0.002396 (0.000260 to 0.005000) | 0.002045 (0.000000 to 0.005070) | 0.011000 (0.001100 to 0.066340) | 0.005500 (0.000000 to 0.019000) |
| IFNg+IL2-TNFa+, DENV-2, NS3-2, Day 120 | 0.002456 (0.000250 to 0.005980) | 0.001800 (0.000000 to 0.003200) | 0.092920 (0.038250 to 0.160000) | 0.153500 (0.048520 to 0.353170) |

| | | | | |
|---|---|---|---|---|
| IFNg+IL2-TNFa+, DENV-2, NS5-2, Day 120 | 0.001590 (0.000000 to 0.002636) | 0.000702 (0.000000 to 0.002960) | 0.094740 (0.030050 to 0.205000) | 0.096615 (0.031580 to 0.220000) |
| IFNg-IL2+TNFa+, DENV-2, NS1-2, Day 120 | 0.005710 (0.000000 to 0.010000) | 0.008335 (0.002900 to 0.017000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa+, DENV-2, NS3-2, Day 120 | 0.000000 (0.000000 to 0.005520) | 0.000000 (0.000000 to 0.004000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa+, DENV-2, NS5-2, Day 120 | 0.003580 (0.000000 to 0.008000) | 0.003275 (0.000000 to 0.010660) | 0.00000 (0.00000 to 0.00000) | 0.00000 (0.00000 to 0.001250) |
| IFNg+IL2-TNFa-, DENV-2, NS1-2, Day 120 | 0.002490 (0.000000 to 0.005560) | 0.001520 (0.000000 to 0.004380) | 0.006000 (0.001770 to 0.019000) | 0.003750 (0.000000 to 0.007240) |
| IFNg+IL2-TNFa-, DENV-2, NS3-2, Day 120 | 0.001620 (0.000000 to 0.002630) | 0.000365 (0.000000 to 0.002000) | 0.033420 (0.009000 to 0.081860) | 0.039000 (0.015000 to 0.104850) |
| IFNg+IL2-TNFa-, DENV-2, NS5-2, Day 120 | 0.000000 (0.000000 to 0.002000) | 0.000205 (0.000000 to 0.002830) | 0.022820 (0.012340 to 0.058000) | 0.018425 (0.004130 to 0.060560) |
| IFNg-IL2+TNFa-, DENV-2, NS1-2, Day 120 | 0.010000 (0.000000 to 0.015000) | 0.007000 (0.000000 to 0.012000) | 0.000000 (0.000000 to 0.008000) | 0.002000 (0.000000 to 0.017000) |
| IFNg-IL2+TNFa-, DENV-2, NS3-2, Day 120 | 0.000000 (0.000000 to 0.005000) | 0.001500 (0.000000 to 0.011000) | 0.005000 (0.000000 to 0.017000) | 0.000000 (0.000000 to 0.012000) |
| IFNg-IL2+TNFa-, DENV-2, NS5-2, Day 120 | 0.001000 (0.000000 to 0.013000) | 0.000000 (0.000000 to 0.013000) | 0.005000 (0.000000 to 0.015000) | 0.000000 (0.000000 to 0.014000) |
| IFNg-IL2-TNFa+, DENV-2, NS1-2, Day 120 | 0.001000 (0.000000 to 0.020000) | 0.002000 (0.000000 to 0.030000) | 0.004000 (0.000000 to 0.017000) | 0.003000 (0.000000 to 0.020000) |
| IFNg-IL2-TNFa+, DENV-2, NS3-2, Day 120 | 0.000000 (0.000000 to 0.030000) | 0.000000 (0.000000 to 0.028000) | 0.010000 (0.000000 to 0.020000) | 0.016500 (0.000000 to 0.033000) |
| IFNg-IL2-TNFa+, DENV-2, NS5-2, Day 120 | 0.020000 (0.000000 to 0.050000) | 0.015000 (0.000000 to 0.049000) | 0.013000 (0.000000 to 0.027340) | 0.011000 (0.000000 to 0.031000) |
| IFNg+IL2+TNFa+, DENV-2, NS1-2, Day 270 | 0.009090 (0.003610 to 0.016000) | 0.006190 (0.002930 to 0.015000) | 0.000000 (0.000000 to 0.003860) | 0.000000 (0.000000 to 0.002300) |
| IFNg+IL2+TNFa+, DENV-2, NS3-2, Day 270 | 0.004950 (0.001750 to 0.007780) | 0.001510 (0.000000 to 0.004546) | 0.006680 (0.000000 to 0.020000) | 0.004630 (0.001540 to 0.009370) |
| IFNg+IL2+TNFa+, DENV-2, NS5-2, Day 270 | 0.002890 (0.001910 to 0.004530) | 0.002466 (0.000000 to 0.005780) | 0.007480 (0.001650 to 0.030780) | 0.003690 (0.001120 to 0.019000) |
| IFNg+IL2+TNFa-, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.001320) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2+TNFa-, DENV-2, NS3-2, Day 270 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.002690) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2+TNFa-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001220) | 0.000000 (0.000000 to 0.001540) |
| IFNg+IL2-TNFa+, DENV-2, NS1-2, Day 270 | 0.000200 (0.000000 to 0.002270) | 0.001240 (0.000000 to 0.003680) | 0.007010 (0.002000 to 0.041450) | 0.003640 (0.000000 to 0.020000) |
| IFNg+IL2-TNFa+, DENV-2, NS3-2, Day 270 | 0.002290 (0.000000 to 0.005380) | 0.000640 (0.000000 to 0.002180) | 0.073630 (0.033000 to 0.189000) | 0.104740 (0.035840 to 0.275040) |

| | | | | |
|---|---|---|---|---|
| IFNg+IL2-TNFa+, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.001940) | 0.000334 (0.000000 to 0.002990) | 0.101450 (0.022180 to 0.197960) | 0.061030 (0.022000 to 0.212030) |
| IFNg-IL2+TNFa+, DENV-2, NS1-2, Day 270 | 0.003000 (0.001000 to 0.013000) | 0.005330 (0.001370 to 0.010000) | 0.000000 (0.000000 to 0.000010) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa+, DENV-2, NS3-2, Day 270 | 0.001030 (0.000000 to 0.005780) | 0.001320 (0.000000 to 0.004830) | 0.000000 (0.000000 to 0.001340) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa+, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.004000) | 0.002090 (0.000000 to 0.007050) | 0.000000 (0.000000 to 0.001340) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2-TNFa-, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.002940) | 0.000000 (0.000000 to 0.002060) | 0.006890 (0.000000 to 0.017270) | 0.001670 (0.000000 to 0.008070) |
| IFNg+IL2-TNFa-, DENV-2, NS3-2, Day 270 | 0.000000 (0.000000 to 0.002860) | 0.000000 (0.000000 to 0.001630) | 0.015000 (0.004570 to 0.029000) | 0.016140 (0.001430 to 0.048550) |
| IFNg+IL2-TNFa-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.003550) | 0.000000 (0.000000 to 0.001350) | 0.018200 (0.006240 to 0.033830) | 0.009180 (0.000000 to 0.025120) |
| IFNg-IL2+TNFa-, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.012000) | 0.001000 (0.000000 to 0.008000) | 0.002000 (0.000000 to 0.009000) | 0.001000 (0.000000 to 0.005360) |
| IFNg-IL2+TNFa-, DENV-2, NS3-2, Day 270 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001980) | 0.001000 (0.000000 to 0.009000) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.003000) | 0.000000 (0.000000 to 0.006000) | 0.000000 (0.000000 to 0.008000) | 0.000000 (0.000000 to 0.006000) |
| IFNg-IL2-TNFa+, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.010000) | 0.000000 (0.000000 to 0.020000) | 0.011000 (0.000000 to 0.024000) | 0.000000 (0.000000 to 0.015000) |
| IFNg-IL2-TNFa+, DENV-2, NS3-2, Day 270 | 0.010000 (0.000000 to 0.030000) | 0.005000 (0.000000 to 0.037000) | 0.020000 (0.000000 to 0.042000) | 0.010000 (0.000000 to 0.055000) |
| IFNg-IL2-TNFa+, DENV-2, NS5-2, Day 270 | 0.001000 (0.000000 to 0.050000) | 0.000000 (0.000000 to 0.027000) | 0.021000 (0.001000 to 0.047000) | 0.011000 (0.000000 to 0.033000) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phenotype Characterization of Cellular Immune Response by Percentage of Total T Cells DENV-2 NS Proteins at 1 Month Post First, 1 and 6 Months Post Second Vaccination, by Dengue Baseline Seropositivity Status

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|---|---|
| End point title | Phenotype Characterization of Cellular Immune Response by Percentage of Total T Cells DENV-2 NS Proteins at 1 Month Post First, 1 and 6 Months Post Second Vaccination, by Dengue Baseline Seropositivity Status |

End point description:

Phenotype characterization of cellular immune response by dengue Baseline seropositivity status assessed by frequency of total CD4+ and CD8+ T cells and was performed in subset of participants with IFN- γ ELISPOT responses >500 SFC/million cells and availability of sufficient cells. Seropositive: reciprocal neutralizing titer (MNT50) >=10 for one or more dengue serotypes. Seronegative: titer value of <10 for all 4 serotypes. Peptide pools included NS for DENV-2 serotype. Data are presented fo different expression profiles of IFN-γ, IL-2 and TNF-α cytokines for each peptide pool. Data is reported per Baseline seropositivity status (Seropositive and Seronegative) based on type of T cells present in participants at time of analysis (CD4+ and CD8+ T cells). ICS Subset 'by Baseline seropositivity status

based on T-cells'. Number analysed:participants with data available for analysis for specific category.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); 1and 6 months post second vaccination (Days 120 Days 270)

| **End point values** | TDV 0.5 mL: Seropositive: CD4+ T-Cells | TDV 0.5 mL: Seronegative: CD4+ T-Cells | TDV 0.5 mL: Seropositive: CD8+ T- Cells | TDV 0.5 mL: Seronegative: CD8+ T-Cells |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 44 | 35 | 44 | 35 |
| Units: percentage of T cells | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| IFNg+IL2+TNFa+, DENV-2, NS1-2, Day 30 | 0.013745 (0.005555 to 0.023190) | 0.008110 (0.001850 to 0.012000) | 0.002485 (0.000000 to 0.008035) | 0.000000 (0.000000 to 0.011000) |
| IFNg+IL2+TNFa+, DENV-2, NS3-2, Day 30 | 0.005720 (0.001970 to 0.015000) | 0.005000 (0.002300 to 0.009290) | 0.020500 (0.002375 to 0.037175) | 0.020000 (0.006800 to 0.041000) |
| IFNg+IL2+TNFa+, DENV-2, NS5-2, Day 30 | 0.005525 (0.002520 to 0.012000) | 0.005380 (0.002890 to 0.009420) | 0.020175 (0.002295 to 0.053500) | 0.011000 (0.004400 to 0.031000) |
| IFNg+IL2+TNFa-, DENV-2, NS1-2, Day 30 | 0.000000 (0.000000 to 0.001071) | 0.000000 (0.000000 to 0.001350) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2+TNFa-, DENV-2, NS3-2, Day 30 | 0.000000 (0.000000 to 0.001047) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.002645) | 0.001370 (0.000000 to 0.003000) |
| IFNg+IL2+TNFa-, DENV-2, NS5-2, Day 30 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001030) | 0.001515 (0.000000 to 0.004265) | 0.001770 (0.000000 to 0.005340) |
| IFNg+IL2-TNFa+, DENV-2, NS1-2, Day 30 | 0.004800 (0.000835 to 0.008530) | 0.003540 (0.000380 to 0.006230) | 0.019145 (0.000420 to 0.067605) | 0.012900 (0.000190 to 0.032000) |
| IFNg+IL2-TNFa+, DENV-2, NS3-2, Day 30 | 0.002830 (0.000000 to 0.007420) | 0.002960 (0.001120 to 0.005090) | 0.121135 (0.045870 to 0.469050) | 0.186520 (0.067540 to 0.435160) |
| IFNg+IL2-TNFa+, DENV-2, NS5-2, Day 30 | 0.003085 (0.001255 to 0.005765) | 0.004110 (0.000000 to 0.007100) | 0.162115 (0.028000 to 0.344500) | 0.127550 (0.046350 to 0.512900) |
| IFNg-IL2+TNFa+, DENV-2, NS1-2, Day 30 | 0.003945 (0.000000 to 0.011215) | 0.002310 (0.000000 to 0.006270) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa+, DENV-2, NS3-2, Day 30 | 0.002130 (0.000000 to 0.007810) | 0.001230 (0.000000 to 0.004790) | 0.000000 (0.000000 to 0.000155) | 0.000000 (0.000000 to 0.001020) |
| IFNg-IL2+TNFa+, DENV-2, NS5-2, Day 30 | 0.003790 (0.000500 to 0.007985) | 0.002270 (0.000000 to 0.008000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2-TNFa-, DENV-2, NS1-2, Day 30 | 0.000630 (0.000000 to 0.003095) | 0.000570 (0.000000 to 0.004640) | 0.007750 (0.001750 to 0.032860) | 0.007160 (0.002000 to 0.027540) |
| IFNg+IL2-TNFa-, DENV-2, NS3-2, Day 30 | 0.000165 (0.000000 to 0.003210) | 0.000130 (0.000000 to 0.002580) | 0.060770 (0.012905 to 0.163835) | 0.050000 (0.029540 to 0.255820) |
| IFNg+IL2-TNFa-, DENV-2, NS5-2, Day 30 | 0.000450 (0.000000 to 0.003105) | 0.000960 (0.000000 to 0.003680) | 0.053260 (0.019500 to 0.115390) | 0.105000 (0.014920 to 0.230980) |

| | | | | |
|---|---|---|---|---|
| IFNg-IL2+TNFa-, DENV-2, NS1-2, Day 30 | 0.001500 (0.000000 to 0.009500) | 0.000000 (0.000000 to 0.009000) | 0.002500 (0.000000 to 0.008000) | 0.002000 (0.000000 to 0.010000) |
| IFNg-IL2+TNFa-, DENV-2, NS3-2, Day 30 | 0.000000 (0.000000 to 0.009000) | 0.000000 (0.000000 to 0.002000) | 0.001000 (0.000000 to 0.008200) | 0.000000 (0.000000 to 0.008220) |
| IFNg-IL2+TNFa-, DENV-2, NS5-2, Day 30 | 0.001000 (0.000000 to 0.010000) | 0.000000 (0.000000 to 0.008000) | 0.000000 (0.000000 to 0.010000) | 0.004000 (0.000000 to 0.009000) |
| IFNg-IL2-TNFa+, DENV-2, NS1-2, Day 30 | 0.004500 (0.000000 to 0.035000) | 0.000000 (0.000000 to 0.014000) | 0.004500 (0.000000 to 0.018000) | 0.000000 (0.000000 to 0.004000) |
| IFNg-IL2-TNFa+, DENV-2, NS3-2, Day 30 | 0.010000 (0.000000 to 0.045000) | 0.006000 (0.000000 to 0.030000) | 0.017500 (0.002000 to 0.033000) | 0.005000 (0.000000 to 0.020000) |
| IFNg-IL2-TNFa+, DENV-2, NS5-2, Day 30 | 0.033000 (0.000000 to 0.070000) | 0.000000 (0.000000 to 0.032000) | 0.013500 (0.000000 to 0.032000) | 0.000000 (0.000000 to 0.027000) |
| IFNg+IL2+TNFa+, DENV-2, NS1-2, Day 120 | 0.011000 (0.003860 to 0.017000) | 0.005531 (0.003340 to 0.016010) | 0.001400 (0.000000 to 0.004030) | 0.001320 (0.000000 to 0.004240) |
| IFNg+IL2+TNFa+, DENV-2, NS3-2, Day 120 | 0.003480 (0.000000 to 0.008830) | 0.003300 (0.001670 to 0.005510) | 0.010000 (0.002650 to 0.028000) | 0.010000 (0.002740 to 0.015000) |
| IFNg+IL2+TNFa+, DENV-2, NS5-2, Day 120 | 0.002705 (0.000000 to 0.005470) | 0.001460 (0.000000 to 0.003000) | 0.012000 (0.002670 to 0.035000) | 0.006000 (0.002230 to 0.013000) |
| IFNg+IL2+TNFa-, DENV-2, NS1-2, Day 120 | 0.000975 (0.000000 to 0.002670) | 0.001220 (0.000000 to 0.001840) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2+TNFa-, DENV-2, NS3-2, Day 120 | 0.000000 (0.000000 to 0.001580) | 0.000000 (0.000000 to 0.001150) | 0.000000 (0.000000 to 0.001920) | 0.000000 (0.000000 to 0.001460) |
| IFNg+IL2+TNFa-, DENV-2, NS5-2, Day 120 | 0.000000 (0.000000 to 0.000908) | 0.000000 (0.000000 to 0.000953) | 0.001540 (0.000000 to 0.003450) | 0.000000 (0.000000 to 0.001650) |
| IFNg+IL2-TNFa+, DENV-2, NS1-2, Day 120 | 0.002885 (0.000760 to 0.005320) | 0.002070 (0.000000 to 0.003680) | 0.007155 (0.000000 to 0.036000) | 0.007850 (0.000000 to 0.028000) |
| IFNg+IL2-TNFa+, DENV-2, NS3-2, Day 120 | 0.002915 (0.001090 to 0.004370) | 0.000450 (0.000000 to 0.002670) | 0.144565 (0.039110 to 0.447000) | 0.093000 (0.053410 to 0.163270) |
| IFNg+IL2-TNFa+, DENV-2, NS5-2, Day 120 | 0.000702 (0.000000 to 0.003690) | 0.001570 (0.000000 to 0.002150) | 0.102525 (0.039880 to 0.291210) | 0.078900 (0.025190 to 0.134400) |
| IFNg-IL2+TNFa+, DENV-2, NS1-2, Day 120 | 0.004735 (0.000280 to 0.013000) | 0.011430 (0.003910 to 0.017000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa+, DENV-2, NS3-2, Day 120 | 0.000530 (0.000000 to 0.005520) | 0.000000 (0.000000 to 0.003730) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001140) |
| IFNg-IL2+TNFa+, DENV-2, NS5-2, Day 120 | 0.003100 (0.000000 to 0.007000) | 0.006490 (0.000000 to 0.010660) | 0.000000 (0.000000 to 0.001420) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2-TNFa-, DENV-2, NS1-2, Day 120 | 0.001520 (0.000000 to 0.004710) | 0.002490 (0.000000 to 0.005030) | 0.004280 (0.001060 to 0.009270) | 0.004080 (0.000000 to 0.016790) |
| IFNg+IL2-TNFa-, DENV-2, NS3-2, Day 120 | 0.001235 (0.000000 to 0.002480) | 0.000190 (0.000000 to 0.002720) | 0.046825 (0.015000 to 0.111210) | 0.024000 (0.000000 to 0.056110) |
| IFNg+IL2-TNFa-, DENV-2, NS5-2, Day 120 | 0.000020 (0.000000 to 0.002480) | 0.000000 (0.000000 to 0.002260) | 0.034610 (0.011000 to 0.101210) | 0.016280 (0.006480 to 0.030630) |

| | | | | |
|---|---|---|---|---|
| IFNg-IL2+TNFa-, DENV-2, NS1-2, Day 120 | 0.009500 (0.000000 to 0.011000) | 0.006000 (0.000000 to 0.015000) | 0.001500 (0.000000 to 0.017000) | 0.002000 (0.000000 to 0.014000) |
| IFNg-IL2+TNFa-, DENV-2, NS3-2, Day 120 | 0.000000 (0.000000 to 0.007000) | 0.002000 (0.000000 to 0.011000) | 0.000500 (0.000000 to 0.019000) | 0.003000 (0.000000 to 0.012000) |
| IFNg-IL2+TNFa-, DENV-2, NS5-2, Day 120 | 0.000000 (0.000000 to 0.013000) | 0.000000 (0.000000 to 0.013000) | 0.000000 (0.000000 to 0.011000) | 0.006000 (0.000000 to 0.020000) |
| IFNg-IL2-TNFa+, DENV-2, NS1-2, Day 120 | 0.007000 (0.000000 to 0.040000) | 0.000000 (0.000000 to 0.019000) | 0.004500 (0.000000 to 0.028000) | 0.000000 (0.000000 to 0.014000) |
| IFNg-IL2-TNFa+, DENV-2, NS3-2, Day 120 | 0.008000 (0.000000 to 0.030000) | 0.000000 (0.000000 to 0.028000) | 0.018000 (0.000000 to 0.034000) | 0.009000 (0.000000 to 0.019000) |
| IFNg-IL2-TNFa+, DENV-2, NS5-2, Day 120 | 0.020000 (0.000000 to 0.050000) | 0.010000 (0.000000 to 0.040000) | 0.016500 (0.000000 to 0.040000) | 0.008000 (0.000000 to 0.023050) |
| IFNg+IL2+TNFa+, DENV-2, NS1-2, Day 270 | 0.009520 (0.004340 to 0.022820) | 0.004410 (0.002620 to 0.012000) | 0.000000 (0.000000 to 0.002800) | 0.000000 (0.000000 to 0.002390) |
| IFNg+IL2+TNFa+, DENV-2, NS5-2, Day 270 | 0.002890 (0.000334 to 0.005160) | 0.002840 (0.000030 to 0.005730) | 0.005070 (0.001500 to 0.026000) | 0.004940 (0.000000 to 0.016000) |
| IFNg+IL2+TNFa+, DENV-2, NS3-2, Day 270 | 0.003410 (0.000000 to 0.006810) | 0.002330 (0.000190 to 0.005380) | 0.008760 (0.002480 to 0.020000) | 0.003020 (0.000000 to 0.008470) |
| IFNg+IL2+TNFa-, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2+TNFa-, DENV-2, NS3-2, Day 270 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001830) | 0.000000 (0.000000 to 0.000000) |
| IFNg+IL2+TNFa-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001570) | 0.000000 (0.000000 to 0.001170) |
| IFNg+IL2-TNFa+, DENV-2, NS1-2, Day 270 | 0.001660 (0.000000 to 0.004540) | 0.000080 (0.000000 to 0.002160) | 0.004600 (0.000090 to 0.024000) | 0.007010 (0.000000 to 0.023950) |
| IFNg+IL2-TNFa+, DENV-2, NS3-2, Day 270 | 0.001470 (0.000000 to 0.003600) | 0.001790 (0.000000 to 0.003280) | 0.104740 (0.036000 to 0.297940) | 0.080870 (0.029000 to 0.189000) |
| IFNg+IL2-TNFa+, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.002500) | 0.001070 (0.000000 to 0.002810) | 0.070000 (0.029000 to 0.258000) | 0.062400 (0.020880 to 0.135040) |
| IFNg-IL2+TNFa+, DENV-2, NS1-2, Day 270 | 0.004000 (0.000000 to 0.009560) | 0.006000 (0.001370 to 0.014040) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa+, DENV-2, NS3-2, Day 270 | 0.000000 (0.000000 to 0.005560) | 0.001350 (0.000000 to 0.004830) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.000000) |
| IFNg-IL2+TNFa+, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.004190) | 0.002640 (0.000000 to 0.006150) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.001590) |
| IFNg+IL2-TNFa-, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.002940) | 0.000000 (0.000000 to 0.001240) | 0.003620 (0.000000 to 0.011000) | 0.004000 (0.000000 to 0.008430) |
| IFNg+IL2-TNFa-, DENV-2, NS3-2, Day 270 | 0.000080 (0.000000 to 0.002860) | 0.000000 (0.000000 to 0.001600) | 0.023630 (0.001910 to 0.032080) | 0.006880 (0.002440 to 0.016140) |
| IFNg+IL2-TNFa-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.003160) | 0.000000 (0.000000 to 0.002170) | 0.013750 (0.000000 to 0.031280) | 0.009000 (0.003400 to 0.027560) |

| | | | | |
|---|---|---|---|---|
| IFNg-IL2+TNFa-, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.007240) | 0.001000 (0.000000 to 0.011000) | 0.000000 (0.000000 to 0.005360) | 0.001000 (0.000000 to 0.009000) |
| IFNg-IL2+TNFa-, DENV-2, NS3-2, Day 270 | 0.000000 (0.000000 to 0.004240) | 0.000000 (0.000000 to 0.000000) | 0.000000 (0.000000 to 0.003460) | 0.000000 (0.000000 to 0.005000) |
| IFNg-IL2+TNFa-, DENV-2, NS5-2, Day 270 | 0.000000 (0.000000 to 0.006000) | 0.000000 (0.000000 to 0.004000) | 0.000000 (0.000000 to 0.007460) | 0.000000 (0.000000 to 0.006000) |
| IFNg-IL2-TNFa+, DENV-2, NS1-2, Day 270 | 0.000000 (0.000000 to 0.020000) | 0.000000 (0.000000 to 0.010000) | 0.005000 (0.000000 to 0.029000) | 0.002000 (0.000000 to 0.015000) |
| IFNg-IL2-TNFa+, DENV-2, NS3-2, Day 270 | 0.019000 (0.000000 to 0.050000) | 0.000000 (0.000000 to 0.013000) | 0.033000 (0.006000 to 0.072000) | 0.005000 (0.000000 to 0.032000) |
| IFNg-IL2-TNFa+, DENV-2, NS5-2, Day 270 | 0.009000 (0.000000 to 0.050000) | 0.000000 (0.000000 to 0.020000) | 0.020000 (0.006000 to 0.051000) | 0.015000 (0.000000 to 0.025000) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers (GMT) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post First Vaccination, Pre Second Vaccination, and 1, 6 Months Post Second Vaccination and Then Annually Up to 3 Years

| | |
|---|---|
| End point title | Geometric Mean Titers (GMT) of Neutralizing Antibodies for Each of the 4 Dengue Serotypes at 1 Month Post First Vaccination, Pre Second Vaccination, and 1, 6 Months Post Second Vaccination and Then Annually Up to 3 Years |

End point description:

GMT of neutralizing antibodies was measured by microneutralization test (MTN). The dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. PPS included all participants from the FAS who have no major protocol violations. Number analysed is the number of participants with data available for analysis at the given timepoint.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

1 month post first vaccination (Day 30); pre second vaccination (Day 90); 1 and 6 months post second vaccination (Days 120 and 270); annually up to 3 years (Years 1, 2 and 3)

| **End point values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195 | | | |
| Units: titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| DENV-1, Day 30 | 402.3 (287.5 to 562.9) | | | |
| DENV-2, Day 30 | 5482.2 (4626.4 to 6496.3) | | | |

| | | | | |
|---|---|---|---|---|
| DENV-3, Day 30 | 436.1 (326.9 to 581.7) | | | |
| DENV-4, Day 30 | 253.9 (182.6 to 353.1) | | | |
| DENV-1, Day 90 | 271.7 (193.9 to 380.7) | | | |
| DENV-2, Day 90 | 2736.3 (2295.1 to 3262.5) | | | |
| DENV-3, Day 90 | 218.7 (162.0 to 295.2) | | | |
| DENV-4, Day 90 | 177.4 (129.6 to 242.8) | | | |
| DENV-1, Day 120 | 550.6 (408.0 to 743.1) | | | |
| DENV-2, Day 120 | 2808.2 (2395.0 to 3292.8) | | | |
| DENV-3, Day 120 | 404.2 (312.6 to 522.7) | | | |
| DENV-4, Day 120 | 427.1 (335.4 to 543.8) | | | |
| DENV-1, Day 270 | 343.3 (249.8 to 471.6) | | | |
| DENV-2, Day 270 | 1729.9 (1435.7 to 2084.4) | | | |
| DENV-3, Day 270 | 203.8 (153.5 to 270.7) | | | |
| DENV-4, Day 270 | 186.6 (141.6 to 246.0) | | | |
| DENV-1, Year 1 | 243.8 (176.4 to 337.0) | | | |
| DENV-2, Year 1 | 896.2 (729.9 to 1100.5) | | | |
| DENV-3, Year 1 | 148.6 (111.6 to 197.7) | | | |
| DENV-4, Year 1 | 142.4 (108.8 to 186.3) | | | |
| DENV-1, Year 2 | 290.8 (200.8 to 421.1) | | | |
| DENV-2, Year 2 | 724.7 (564.2 to 930.8) | | | |
| DENV-3, Year 2 | 172.7 (120.6 to 247.1) | | | |
| DENV-4, Year 2 | 157.7 (114.0 to 218.0) | | | |
| DENV-1, Year 3 | 178.7 (127.3 to 250.8) | | | |
| DENV-2, Year 3 | 546.4 (435.2 to 686.0) | | | |
| DENV-3, Year 3 | 125.2 (92.8 to 169.0) | | | |
| DENV-4, Year 3 | 91.6 (69.4 to 120.7) | | | |

**Statistical analyses**

No statistical analyses for this end point

## Secondary: Percentage of Participants Seropositive for Each of the 4 Dengue Serotypes at 1 Month Post First Vaccination, Pre-second Vaccination, and 1, 6 Months Post Second Vaccination and Then Annually up to 3 Years

| End point title | Percentage of Participants Seropositive for Each of the 4 Dengue Serotypes at 1 Month Post First Vaccination, Pre-second Vaccination, and 1, 6 Months Post Second Vaccination and Then Annually up to 3 Years |
|---|---|

End point description:

Seropositive was defined as a reciprocal neutralizing titer ≥10. The dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. PPS included all participants from the FAS who have no major protocol violations. Number analysed is the number of participants with data available at the given timepoint.

| End point type | Secondary |
|---|---|

End point timeframe:

1 month post first vaccination (Day 30); pre second vaccination (Day 90); 1 and 6 months post second vaccination (Days 120 and 270); annually up to 3 years (Years 1, 2 and 3)

| **End point values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| DENV-1, Day 30 | 96.8 (93.1 to 98.8) | | | |
| DENV-2, Day 30 | 99.5 (97.0 to 100.0) | | | |
| DENV-3, Day 30 | 99.5 (97.0 to 100.0) | | | |
| DENV-4, Day 30 | 93.0 (88.3 to 96.2) | | | |
| DENV-1, Day 90 | 90.8 (85.8 to 94.4) | | | |
| DENV-2, Day 90 | 99.5 (97.2 to 100.0) | | | |
| DENV-3, Day 90 | 94.4 (90.1 to 97.2) | | | |
| DENV-4, Day 90 | 91.8 (87.0 to 95.2) | | | |
| DENV-1, Day 120 | 99.5 (97.0 to 100.0) | | | |
| DENV-2, Day 120 | 100.0 (98.0 to 100.0) | | | |
| DENV-3, Day 120 | 100.0 (98.0 to 100.0) | | | |
| DENV-4, Day 120 | 100.0 (98.0 to 100.0) | | | |
| DENV-1, Day 270 | 96.8 (93.1 to 98.8) | | | |
| DENV-2, Day 270 | 100.0 (98.0 to 100.0) | | | |
| DENV-3, Day 270 | 97.9 (94.6 to 99.4) | | | |

| | | | | |
|---|---|---|---|---|
| DENV-4, Day 270 | 96.8 (93.1 to 98.8) | | | |
| DENV-1, Year 1 | 91.1 (86.2 to 94.8) | | | |
| DENV-2, Year 1 | 100.0 (98.1 to 100.0) | | | |
| DENV-3, Year 1 | 93.8 (89.3 to 96.7) | | | |
| DENV-4, Year 1 | 96.4 (92.6 to 98.5) | | | |
| DENV-1, Year 2 | 93.5 (88.4 to 96.8) | | | |
| DENV-2, Year 2 | 100.0 (97.6 to 100.0) | | | |
| DENV-3, Year 2 | 89.6 (83.7 to 93.9) | | | |
| DENV-4, Year 2 | 95.5 (90.9 to 98.2) | | | |
| DENV-1, Year 3 | 84.4 (78.3 to 89.4) | | | |
| DENV-2, Year 3 | 100.0 (98.0 to 100.0) | | | |
| DENV-3, Year 3 | 86.7 (80.8 to 91.3) | | | |
| DENV-4, Year 3 | 86.1 (80.2 to 90.8) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Seropositive for Multiple Dengue Serotypes at 1 Month Post First Vaccination, Pre Second Vaccination, 1, 6 Months Post Second Vaccination and Annually up to 3 Years

| | |
|---|---|
| End point title | Percentage of Participants Seropositive for Multiple Dengue Serotypes at 1 Month Post First Vaccination, Pre Second Vaccination, 1, 6 Months Post Second Vaccination and Annually up to 3 Years |

End point description:

Seropositive was defined as a reciprocal neutralizing titer ≥10. The dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Seropositive for multiple dengue serotypes were summarized in the following categories: tetravalent and at least trivalent. Seropositive was defined as a reciprocal neutralizing titer ≥10. The dengue virus serotypes are DENV-1, DENV-2, DENV-3 and DENV-4. Seropositive for multiple dengue serotypes were summarized in the following categories: tetravalent and at least trivalent.PPS included all participants from the FAS who have no major protocol violations. Number analysed is the number of participants with data available for analysis at the given timepoint.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

1 month post first vaccination (Day 30); pre second vaccination (Day 90); 1 and 6 months post second vaccination (Days 120 and 270); annually up to 3 years (Years 1, 2 and 3)

| End point values | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 195 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Tetravalent, Day 30 | 90.8 (85.7 to 94.6) | | | |
| At Least Trivalent, Day 30 | 98.4 (95.3 to 99.7) | | | |
| Tetravalent, Day 90 | 83.6 (77.6 to 88.5) | | | |
| At Least Trivalent, Day 90 | 95.4 (91.4 to 97.9) | | | |
| Tetravalent, Day 120 | 99.5 (97.0 to 100.0) | | | |
| At Least Trivalent, Day 120 | 100.0 (98.0 to 100.0) | | | |
| Tetravalent, Day 270 | 93.0 (88.4 to 96.2) | | | |
| At Least Trivalent, Day 270 | 98.4 (95.4 to 99.7) | | | |
| Tetravalent, Year 1 | 87.5 (82.0 to 91.8) | | | |
| At Least Trivalent, Year 1 | 95.3 (91.3 to 97.8) | | | |
| Tetravalent, Year 2 | 86.4 (79.9 to 91.4) | | | |
| At Least Trivalent, Year 2 | 93.5 (88.4 to 96.8) | | | |
| Tetravalent, Year 3 | 76.7 (69.8 to 82.6) | | | |
| At Least Trivalent, Year 3 | 87.2 (81.4 to 91.7) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Experiencing Unsolicited Adverse Events (AE)

| End point title | Percentage of Participants Experiencing Unsolicited Adverse Events (AE) |
|---|---|

End point description:

An AE was defined as any untoward medical occurrence in a clinical investigation participant administered a trial vaccine; it does not necessarily have to have a causal relationship with trial vaccine administration. Safety Set included all enrolled participants who received at least 1 dose of TDV. Number analysed is the number of participants with data available for analysis at the given timepoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 28 days (day of vaccination + 27 days) after administration of each vaccine dose on Day 1 [Month 0] and Day 90 [Month 3]

| End point values | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 200 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| After First Vaccination | 26.5 | | | |
| After Second Vaccination | 25.3 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Medically Attended AEs (MAAEs)

| End point title | Percentage of Participants With Medically Attended AEs (MAAEs) |
|---|---|

End point description:

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

| End point type | Secondary |
|---|---|

End point timeframe:

From first vaccination (Day 1) up to 6 months post second vaccination (Day 270)

| End point values | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 200 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 50.5 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Serious Adverse Events (SAEs)

| End point title | Percentage of Participants With Serious Adverse Events (SAEs) |
|---|---|

End point description:

A SAE was 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 due to other reasons than the above mentioned criteria. Safety Set included all enrolled participants who received at least 1 dose of TDV.

| End point type | Secondary |
|---|---|

End point timeframe:

From first vaccination (Day 1) up to end of study (Approximately 3 years)

| **End point values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 200 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 5.5 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Virologically Confirmed Dengue

| End point title | Percentage of Participants With Virologically Confirmed Dengue |
|---|---|

End point description:

Participants with febrile illness defined as fever ≥38°C on any 2 of 3 consecutive days were evaluated for dengue. Virologically confirmed dengue was defined as febrile illness with a positive serotype-specific RT-PCR (i.e. positive dengue detection RT-PCR). Safety Set included all enrolled participants who received at least 1 dose of TDV.

| End point type | Secondary |
|---|---|

End point timeframe:

From first vaccination (Day 1) up to 6 months post second vaccination (Day 270)

| **End point values** | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 200 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 6.0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and SAEs: From first vaccination(Day 1) up to end of study (Approximately 3 years);Non-SAEs: Up to 28 days (day of vaccination + 27 days) after administration of each vaccine dose on Day 1[Month 0] and Day 90[Month 3]

Adverse event reporting additional description:

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

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|---|---|
| Assessment type | Systematic |

### Dictionary used

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|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 21.0 |

### Reporting groups

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|---|---|
| Reporting group title | Tetravalent Dengue Vaccine (TDV) 0.5 mL |

Reporting group description:

TDV 0.5 mL, subcutaneous (SC) injection, on Day 1 (Month 0) and Day 90 (Month 3).

| **Serious adverse events** | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 200 (5.50%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Social circumstances | | | |
| Victim of sexual abuse | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Faecaloma | | | |
| alternative dictionary used: MedDRA 21.0 | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| alternative dictionary used: MedDRA 21.0 | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Biliary colic | | | |
| alternative dictionary used: MedDRA 21.0 | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 200 (1.50%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Typhoid fever | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dengue fever | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Systemic viral infection | | | |
| subjects affected / exposed | 1 / 200 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Tetravalent Dengue Vaccine (TDV) 0.5 mL | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 66 / 200 (33.00%) | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 29 / 200 (14.50%) | | |
| occurrences (all) | 33 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 20 / 200 (10.00%) | | |
| occurrences (all) | 21 | | |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 12 / 200 (6.00%) | | |
| occurrences (all) | 13 | | |
| Systemic viral infection | | | |
| subjects affected / exposed | 9 / 200 (4.50%) | | |
| occurrences (all) | 9 | | |
| Pneumonia | | | |
| subjects affected / exposed | 8 / 200 (4.00%) | | |
| occurrences (all) | 9 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 4 / 200 (2.00%) | | |
| occurrences (all) | 4 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

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| Analysis of samples collected at Day 90 and at Years 1, 2 and 3 for outcome measures related to assessment of cellular immune response is ongoing due to limited testing capacities of laboratory (COVID-19); data will be reported when available. |

Notes: