



Clinical trial results:

Safety of ChimeriVax™ Dengue Tetravalent Vaccine in Subjects Aged 2 to 45 Years in the Philippines

Summary

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|--------------------------|-------------------|
| EudraCT number | 2014-001534-29 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 11 September 2012 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 16 February 2016 |
| First version publication date | 31 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | CYD05 |
|-----------------------|-------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Sanofi Pasteur SA |
| Sponsor organisation address | 2, avenue Pont Pasteur, Lyon Cedex 07, France, 69367 |
| Public contact | Senior Director, Clinical Development, Sanofi Pasteur SA, 65 6431 2358, Anh.Wartel-Tram@sanofipasteur.com |
| Scientific contact | Senior Director, Clinical Development, Sanofi Pasteur SA, 65 6431 2358, Anh.Wartel-Tram@sanofipasteur.com |

Notes:

Paediatric regulatory details

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|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001201-PIP01-11 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 29 April 2013 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 September 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Safety and reactogenicity

Dengue immune responses and Persistence of antibodies

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment was also available on site in case of any immediate allergic reactions.

Background therapy:

Not applicable

Evidence for comparator:

The Typhim Vi vaccine was chosen as a control vaccine since typhoid fever is endemic in the Philippines and the vaccine is not administered routinely. Therefore, it represented a benefit for the subjects.

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|---|---------------|
| Actual start date of recruitment | 02 March 2006 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 5 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Philippines: 126 |
| Worldwide total number of subjects | 126 |
| 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) | 72 |

| | |
|---------------------------|----|
| Adolescents (12-17 years) | 36 |
| Adults (18-64 years) | 18 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 09 March 2006 to 01 September 2007 at 1 clinical center in the Philippines.

Pre-assignment

Screening details:

A total of 126 subjects who met all of the inclusion criteria and none of the exclusion criteria were enrolled and randomized.

Period 1

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

Blinding implementation details:

The blind-observer approach was used for the first injection to ensure unbiased safety evaluation. Qualified and trained study personnel prepared the vaccines for each subject and were therefore the only ones to know which vaccine was administered at the first injection. The CYD dengue vaccine was used as open-label for the second and third injections in all subjects.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Group 1 |

Arm description:

Subjects received the CYD dengue vaccine for all three injections, one each on Days 0, 105, and 365, respectively.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | ChimeriVax™ Dengue Tetravalent Vaccine |
| Investigational medicinal product code | 323 |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5 mL, subcutaneous use, 3 injections on Days 0, 135, and 365.

| | |
|------------------|---------|
| Arm title | Group 2 |
|------------------|---------|

Arm description:

Subjects received typhoid vaccine (Typhim Vi) as first injection and CYD dengue vaccine as second and third injections 8 to 9 months apart (Days 105 and 365).

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | ChimeriVax™ Dengue Tetravalent Vaccine |
| Investigational medicinal product code | 323 |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5 mL, subcutaneous, 2 injections. One each on Days 105 and 365.

| | |
|--|-----------------|
| Investigational medicinal product name | Typhoid vaccine |
| Investigational medicinal product code | |
| Other name | Typhim Vi |

| | |
|--------------------------|--------------------------|
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5 mL, subcutaneous, 1 injection on Day 0.

| Number of subjects in period 1 | Group 1 | Group 2 |
|---------------------------------------|---------|---------|
| Started | 84 | 42 |
| Completed | 80 | 39 |
| Not completed | 4 | 3 |
| Consent withdrawn by subject | - | 1 |
| Adverse event, non-fatal | 3 | 1 |
| Protocol deviation | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Group 1 |
|-----------------------|---------|

Reporting group description:

Subjects received the CYD dengue vaccine for all three injections, one each on Days 0, 105, and 365, respectively.

| | |
|-----------------------|---------|
| Reporting group title | Group 2 |
|-----------------------|---------|

Reporting group description:

Subjects received typhoid vaccine (Typhim Vi) as first injection and CYD dengue vaccine as second and third injections 8 to 9 months apart (Days 105 and 365).

| Reporting group values | Group 1 | Group 2 | Total |
|---|---------|---------|-------|
| Number of subjects | 84 | 42 | 126 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 48 | 24 | 72 |
| Adolescents (12-17 years) | 24 | 12 | 36 |
| Adults (18-64 years) | 12 | 6 | 18 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 12.2 | 12.2 | |
| standard deviation | ± 8.3 | ± 9.5 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 41 | 27 | 68 |
| Male | 43 | 15 | 58 |
| Study sub-groups by age | | | |
| Study subjects were also categorized into 4 subgroups based on their ages as Adults, Adolescents, and 2 Children groups | | | |
| Units: Subjects | | | |
| Adults (age 18 to 45 years) | 12 | 6 | 18 |
| Adolescents (age 12 to 17 years) | 24 | 12 | 36 |
| Children (age 6 to 11 years) | 24 | 12 | 36 |
| Children (age 2 to 5 years) | 24 | 12 | 36 |

End points

End points reporting groups

| | |
|--|---------|
| Reporting group title | Group 1 |
| Reporting group description: | |
| Subjects received the CYD dengue vaccine for all three injections, one each on Days 0, 105, and 365, respectively. | |
| Reporting group title | Group 2 |
| Reporting group description: | |
| Subjects received typhoid vaccine (Typhim Vi) as first injection and CYD dengue vaccine as second and third injections 8 to 9 months apart (Days 105 and 365). | |

Primary: Percentage of Subjects with Antibody titer ≥ 10 (1/dil) Against Each Serotype with the Parental Dengue Virus Strains Before and Following each Injection with ChimeriVax™ Dengue Tetravalent Vaccine

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|---|--|
| End point title | Percentage of Subjects with Antibody titer ≥ 10 (1/dil) Against Each Serotype with the Parental Dengue Virus Strains Before and Following each Injection with ChimeriVax™ Dengue Tetravalent Vaccine ^[1] |
| End point description: | |
| The immune response against the CYD dengue vaccine was assessed using the Dengue Plaque Reduction Neutralization Test (PRNT). | |
| End point type | Primary |
| End point timeframe: | |
| Day 0 (pre-vaccination) and Day 105 and 365 post-vaccination | |
| 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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome. | |

| End point values | Group 1 | Group 2 | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 84 | 42 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| All subjects; Serotype 1; Pre-Inj. 1 | 54.9 | 63.4 | | |
| All subjects; Serotype 1; Post-Inj. 2 | 80.5 | 75.7 | | |
| All subjects; Serotype 1; Post-Inj. 3 | 93.4 | 100 | | |
| All subjects; Serotype 2; Pre-Inj. 1 | 57.3 | 69 | | |
| All subjects; Serotype 2; Post-Inj. 2 | 96.3 | 82.1 | | |
| All subjects; Serotype 2; Post-Inj. 3 | 98.7 | 100 | | |
| All subjects; Serotype 3; Pre-Inj. 1 | 69.5 | 76.2 | | |
| All subjects; Serotype 3; Post-Inj. 2 | 100 | 94.6 | | |
| All subjects; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| All subjects; Serotype 4; Pre-Inj. 1 | 63.4 | 71.4 | | |
| All subjects; Serotype 4; Post-Inj. 2 | 97.6 | 94.6 | | |
| All subjects; Serotype 4; Post-Inj. 3 | 97.4 | 100 | | |
| 18-45 years; Serotype 1; Pre-Inj. 1 | 100 | 83.3 | | |
| 18-45 years; Serotype 1; Post-Inj. 2 | 100 | 100 | | |

| | | | | |
|--------------------------------------|------|------|--|--|
| 18-45 years; Serotype 1; Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 2; Pre-Inj. 1 | 100 | 100 | | |
| 18-45 years; Serotype 2; Post-Inj. 2 | 100 | 100 | | |
| 18-45 years; Serotype 2; Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 3; Pre-Inj. 1 | 100 | 83.3 | | |
| 18-45 years; Serotype 3; Post-Inj. 2 | 100 | 100 | | |
| 18-45 years; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 4; Pre-Inj. 1 | 100 | 83.3 | | |
| 18-45 years; Serotype 4; Post-Inj. 2 | 100 | 100 | | |
| 18-45 years; Serotype 4; Post-Inj. 3 | 100 | 100 | | |
| 12-17 years; Serotype 1; Pre-Inj. 1 | 70.8 | 83.3 | | |
| 12-17 years; Serotype 1; Post-Inj. 2 | 87.5 | 90.9 | | |
| 12-17 years; Serotype 1; Post-Inj. 3 | 81.8 | 100 | | |
| 12-17 years; Serotype 2; Pre-Inj. 1 | 66.7 | 91.7 | | |
| 12-17 years; Serotype 2; Post-Inj. 2 | 91.7 | 90.9 | | |
| 12-17 years; Serotype 2; Post-Inj. 3 | 95.7 | 100 | | |
| 12-17 years; Serotype 3; Pre-Inj. 1 | 79.2 | 83.3 | | |
| 12-17 years; Serotype 3; Post-Inj. 2 | 100 | 90.9 | | |
| 12-17 years; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| 12-17 years; Serotype 4; Pre-Inj. 1 | 70.8 | 83.3 | | |
| 12-17 years; Serotype 4; Post-Inj. 2 | 95.8 | 90.9 | | |
| 12-17 years; Serotype 4; Post-Inj. 3 | 100 | 100 | | |
| 6-11 years; Serotype 1; Pre-Inj. 1 | 39.1 | 72.7 | | |
| 6-11 years; Serotype 1; Post-Inj. 2 | 75 | 80 | | |
| 6-11 years; Serotype 1; Post-Inj. 3 | 100 | 100 | | |
| 6-11 years; Serotype 2; Pre-Inj. 1 | 47.8 | 58.3 | | |
| 6-11 years; Serotype 2; Post-Inj. 2 | 95.8 | 72.7 | | |
| 6-11 years; Serotype 2; Post-Inj. 3 | 100 | 100 | | |
| 6-11 years; Serotype 3; Pre-Inj. 1 | 56.5 | 83.3 | | |
| 6-11 years; Serotype 3; Post-Inj. 2 | 100 | 100 | | |
| 6-11 years; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| 6-11 years; Serotype 4; Pre-Inj. 1 | 52.2 | 75 | | |
| 6-11 years; Serotype 4; Post-Inj. 2 | 95.8 | 90.9 | | |
| 6-11 years; Serotype 4; Post-Inj. 3 | 100 | 100 | | |
| 2-5 years; Serotype 1; Pre-Inj. 1 | 33.3 | 25 | | |
| 2-5 years; Serotype 1; Post-Inj. 2 | 68.2 | 45.5 | | |
| 2-5 years; Serotype 1; Post-Inj. 3 | 95.5 | 100 | | |
| 2-5 years; Serotype 2; Pre-Inj. 1 | 37.5 | 41.7 | | |
| 2-5 years; Serotype 2; Post-Inj. 2 | 100 | 72.7 | | |
| 2-5 years; Serotype 2; Post-Inj. 3 | 100 | 100 | | |
| 2-5 years; Serotype 3; Pre-Inj. 1 | 58.3 | 58.3 | | |
| 2-5 years; Serotype 3; Post-Inj. 2 | 100 | 88.9 | | |
| 2-5 years; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| 2-5 years; Serotype 4; Pre-Inj. 1 | 50 | 50 | | |
| 2-5 years; Serotype 4; Post-Inj. 2 | 100 | 100 | | |
| 2-5 years; Serotype 4; Post-Inj. 3 | 90.9 | 100 | | |

Statistical analyses

Other pre-specified: Percentage of Subjects with Antibody titer ≥ 10 (1/dil) Against at least 1, 2, 3 or 4 Serotypes with the Parental Dengue Virus Strains Following Injection with ChimeriVax™ Dengue Tetravalent Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects with Antibody titer ≥ 10 (1/dil) Against at least 1, 2, 3 or 4 Serotypes with the Parental Dengue Virus Strains Following Injection with ChimeriVax™ Dengue Tetravalent Vaccine |
|-----------------|---|

End point description:

The immune response against the CYD dengue vaccine was assessed using the Dengue Plaque Reduction Neutralization Test (PRNT).

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|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Day 0 (pre-vaccination) and Days 105 and 365 post-vaccination

| End point values | Group 1 | Group 2 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 84 | 42 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| All subjects; At least 1 serotype (Pre-Inj. 1) | 73.2 | 85.7 | | |
| All subjects; At least 1 serotype (Post-Inj. 2) | 100 | 97.4 | | |
| All subjects; At least 1 serotype (Post-Inj. 3) | 100 | 100 | | |
| All subjects; At least 2 serotypes (Pre-Inj. 1) | 63.4 | 73.8 | | |
| All subjects; At least 2 serotypes (Post-Inj. 2) | 98.8 | 87.2 | | |
| All subjects; At least 2 serotypes (Post-Inj. 3) | 100 | 94.9 | | |
| All subjects; At least 3 serotypes (Pre-Inj. 1) | 57.3 | 64.3 | | |
| All subjects; At least 3 serotypes (Post-Inj. 2) | 96.3 | 76.9 | | |
| All subjects; At least 3 serotypes (Post-Inj. 3) | 98.7 | 84.6 | | |
| All subjects; All 4 serotypes (Pre-Inj. 1) | 51.2 | 54.8 | | |
| All subjects; All 4 serotypes (Post-Inj. 2) | 79.3 | 71.8 | | |
| All subjects; All 4 serotypes (Post-Inj. 3) | 88.5 | 64.1 | | |
| 18-45 years; At least 1 serotype (Pre-Inj. 1) | 100 | 100 | | |
| 18-45 years; At least 1 serotype (Post-Inj. 2) | 100 | 100 | | |
| 18-45 years; At least 1 serotype (Post-Inj. 3) | 100 | 100 | | |
| 18-45 years; At least 2 serotypes (Pre-Inj. 1) | 100 | 83.3 | | |
| 18-45 years; At least 2 serotypes (Post-Inj. 2) | 100 | 100 | | |

| | | | | |
|---|------|------|--|--|
| 18-45 years; At least 2 serotypes (Post-Inj. 3) | 100 | 100 | | |
| 18-45 years; At least 3 serotypes (Pre-Inj. 1) | 100 | 83.3 | | |
| 18-45 years; At least 3 serotypes (Post-Inj. 2) | 100 | 100 | | |
| 18-45 years; At least 3 serotypes (Post-Inj. 3) | 100 | 100 | | |
| 18-45 years; All 4 serotypes (Pre-Inj. 1) | 100 | 83.3 | | |
| 18-45 years; All 4 serotypes (Post-Inj. 2) | 100 | 83.3 | | |
| 18-45 years; All 4 serotypes (Post-Inj. 3) | 88.9 | 83.3 | | |
| 12-17 years; At least 1 serotype (Pre-Inj. 1) | 83.3 | 91.7 | | |
| 12-17 years; At least 1 serotype (Post-Inj. 2) | 100 | 90.9 | | |
| 12-17 years; At least 1 serotype (Post-Inj. 3) | 100 | 100 | | |
| 12-17 years; At least 2 serotypes (Pre-Inj. 1) | 75 | 91.7 | | |
| 12-17 years; At least 2 serotypes (Post-Inj. 2) | 100 | 90.9 | | |
| 12-17 years; At least 2 serotypes (Post-Inj. 3) | 100 | 100 | | |
| 12-17 years; At least 3 serotypes (Pre-Inj. 1) | 66.7 | 83.3 | | |
| 12-17 years; At least 3 serotypes (Post-Inj. 2) | 91.7 | 90.9 | | |
| 12-17 years; At least 3 serotypes (Post-Inj. 3) | 95.7 | 100 | | |
| 12-17 years; All 4 serotypes (Pre-Inj. 1) | 62.5 | 75 | | |
| 12-17 years; All 4 serotypes (Post-Inj. 2) | 83.3 | 90.9 | | |
| 12-17 years; All 4 serotypes (Post-Inj. 3) | 78.3 | 81.8 | | |
| 6-11 years; At least 1 serotype (Pre-Inj. 1) | 65.2 | 91.7 | | |
| 6-11 years; At least 1 serotype (Post-Inj. 2) | 100 | 100 | | |
| 6-11 years; At least 1 serotype (Post-Inj. 3) | 100 | 100 | | |
| 6-11 years; At least 2 serotypes (Pre-Inj. 1) | 47.8 | 75 | | |
| 6-11 years; At least 2 serotypes (Post-Inj. 2) | 95.8 | 90.9 | | |
| 6-11 years; At least 2 serotypes (Post-Inj. 3) | 100 | 90.9 | | |
| 6-11 years; At least 3 serotypes (Pre-Inj. 1) | 47.8 | 58.3 | | |
| 6-11 years; At least 3 serotypes (Post-Inj. 2) | 95.8 | 72.7 | | |
| 6-11 years; At least 3 serotypes (Post-Inj. 3) | 100 | 63.6 | | |
| 6-11 years; All 4 serotypes (Pre-Inj. 1) | 34.8 | 58.3 | | |
| 6-11 years; All 4 serotypes (Post-Inj. 2) | 75 | 72.7 | | |
| 6-11 years; All 4 serotypes (Post-Inj. 3) | 100 | 54.5 | | |
| 2-5 years; At least 1 serotype (Pre-Inj. 1) | 58.3 | 66.7 | | |
| 2-5 years; At least 1 serotype (Post-Inj. 2) | 100 | 100 | | |

| | | | | |
|---|------|------|--|--|
| 2-5 years; At least 1 serotype (Post-Inj. 3) | 100 | 100 | | |
| 2-5 years; At least 2 serotypes (Pre-Inj. 1) | 50 | 50 | | |
| 2-5 years; At least 2 serotypes (Post-Inj. 2) | 100 | 72.7 | | |
| 2-5 years; At least 2 serotypes (Post-Inj. 3) | 100 | 90.9 | | |
| 2-5 years; At least 3 serotypes (Pre-Inj. 1) | 37.5 | 41.7 | | |
| 2-5 years; At least 3 serotypes (Post-Inj. 2) | 100 | 54.5 | | |
| 2-5 years; At least 3 serotypes (Post-Inj. 3) | 100 | 81.8 | | |
| 2-5 years; All 4 serotypes (Pre-Inj. 1) | 33.3 | 16.7 | | |
| 2-5 years; All 4 serotypes (Post-Inj. 2) | 68.2 | 45.5 | | |
| 2-5 years; All 4 serotypes (Post-Inj. 3) | 86.4 | 45.5 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers (GMTs) of Antibodies Against Each Serotype with the Parental Dengue Virus Strain Before and Following Injection with ChimeriVax™ Dengue Tetravalent Vaccine

| | |
|-----------------|---|
| End point title | Geometric Mean Titers (GMTs) of Antibodies Against Each Serotype with the Parental Dengue Virus Strain Before and Following Injection with ChimeriVax™ Dengue Tetravalent Vaccine |
|-----------------|---|

End point description:

Geometric mean titers against each serotype of the Parental Dengue Virus strains were assessed using the Dengue Plaque Reduction Neutralization Test (PRNT).

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Day 0 (pre-vaccination) and Days 105 and 365 post-vaccination

| End point values | Group 1 | Group 2 | | |
|--|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 84 | 42 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| All subjects; Serotype 1; Pre-Inj. 1 | 44 (26.1 to 74.1) | 82.6 (35.7 to 191) | | |
| All subjects; Serotype 1; Post-Inj. 2 | 119 (72.4 to 196) | 170 (73.8 to 391) | | |
| All subjects; Serotype 1; Post-Inj. 3 | 152 (98.4 to 235) | 279 (145 to 538) | | |
| All subjects; Serotype 2; Pre-Inj. 1 | 51.3 (31.1 to 84.7) | 71.7 (36.2 to 142) | | |
| All subjects; Serotype 2; Post-Inj. 2 | 272 (189 to 392) | 185 (91.6 to 375) | | |

| | | | | |
|---------------------------------------|---------------------|---------------------|--|--|
| All subjects; Serotype 2; Post-Inj. 3 | 287 (207 to 398) | 461 (293 to 725) | | |
| All subjects; Serotype 3; Pre-Inj. 1 | 54.1 (35.5 to 82.3) | 107 (54.9 to 210) | | |
| All subjects; Serotype 3; Post-Inj. 2 | 379 (284 to 507) | 380 (210 to 687) | | |
| All subjects; Serotype 3; Post-Inj. 3 | 304 (240 to 385) | 674 (431 to 1052) | | |
| All subjects; Serotype 4; Pre-Inj. 1 | 48.9 (31.6 to 75.9) | 56.6 (31.4 to 102) | | |
| All subjects; Serotype 4; Post-Inj. 2 | 266 (195 to 362) | 241 (140 to 414) | | |
| All subjects; Serotype 4; Post-Inj. 3 | 228 (171 to 303) | 330 (227 to 479) | | |
| 18-45 years; Serotype 1; Pre-Inj. 1 | 208 (106 to 410) | 756 (47.3 to 12069) | | |
| 18-45 years; Serotype 1; Post-Inj. 2 | 626 (381 to 1029) | 2623 (663 to 10377) | | |
| 18-45 years; Serotype 1; Post-Inj. 3 | 315 (183 to 543) | 599 (110 to 3273) | | |
| 18-45 years; Serotype 2; Pre-Inj. 1 | 422 (183 to 974) | 491 (99.3 to 2428) | | |
| 18-45 years; Serotype 2; Post-Inj. 2 | 911 (555 to 1495) | 904 (505 to 1618) | | |
| 18-45 years; Serotype 2; Post-Inj. 3 | 702 (431 to 1145) | 618 (366 to 1042) | | |
| 18-45 years; Serotype 3; Pre-Inj. 1 | 235 (123 to 450) | 334 (31.5 to 3542) | | |
| 18-45 years; Serotype 3; Post-Inj. 2 | 880 (337 to 2297) | 695 (362 to 1335) | | |
| 18-45 years; Serotype 3; Post-Inj. 3 | 593 (347 to 1012) | 482 (253 to 920) | | |
| 18-45 years; Serotype 4; Pre-Inj. 1 | 218 (101 to 472) | 190 (24.7 to 1469) | | |
| 18-45 years; Serotype 4; Post-Inj. 2 | 491 (199 to 1214) | 827 (270 to 2528) | | |
| 18-45 years; Serotype 4; Post-Inj. 3 | 230 (110 to 481) | 533 (205 to 1390) | | |
| 12-17 years; Serotype 1; Pre-Inj. 1 | 112 (38.8 to 324) | 249 (59.2 to 1045) | | |
| 12-17 years; Serotype 1; Post-Inj. 2 | 294 (102 to 849) | 330 (96.7 to 1128) | | |
| 12-17 years; Serotype 1; Post-Inj. 3 | 261 (81.3 to 840) | 504 (166 to 1534) | | |
| 12-17 years; Serotype 2; Pre-Inj. 1 | 92 (34.4 to 246) | 203 (65.9 to 625) | | |
| 12-17 years; Serotype 2; Post-Inj. 2 | 383 (172 to 854) | 312 (95.9 to 1013) | | |
| 12-17 years; Serotype 2; Post-Inj. 3 | 427 (199 to 920) | 528 (220 to 1269) | | |
| 12-17 years; Serotype 3; Pre-Inj. 1 | 85.3 (39.1 to 186) | 259 (63.1 to 1063) | | |
| 12-17 years; Serotype 3; Post-Inj. 2 | 509 (289 to 898) | 352 (81.2 to 1525) | | |
| 12-17 years; Serotype 3; Post-Inj. 3 | 478 (294 to 778) | 827 (367 to 1864) | | |
| 12-17 years; Serotype 4; Pre-Inj. 1 | 55.2 (26.7 to 114) | 83.7 (23.2 to 303) | | |
| 12-17 years; Serotype 4; Post-Inj. 2 | 239 (139 to 409) | 173 (56.1 to 533) | | |
| 12-17 years; Serotype 4; Post-Inj. 3 | 234 (161 to 340) | 241 (139 to 419) | | |

| | | | | |
|-------------------------------------|---------------------|---------------------|--|--|
| 6-11 years; Serotype 1; Pre-Inj. 1 | 19.1 (8.06 to 45.3) | 108 (18.5 to 637) | | |
| 6-11 years; Serotype 1; Post-Inj. 2 | 52.3 (23.7 to 116) | 196 (29 to 1323) | | |
| 6-11 years; Serotype 1; Post-Inj. 3 | 101 (53.2 to 194) | 625 (116 to 3374) | | |
| 6-11 years; Serotype 2; Pre-Inj. 1 | 33.7 (12.2 to 92.5) | 39.9 (11.3 to 141) | | |
| 6-11 years; Serotype 2; Post-Inj. 2 | 220 (107 to 455) | 81.6 (17.8 to 373) | | |
| 6-11 years; Serotype 2; Post-Inj. 3 | 242 (127 to 459) | 364 (101 to 1304) | | |
| 6-11 years; Serotype 3; Pre-Inj. 1 | 35.7 (14.5 to 88) | 92.2 (29.2 to 291) | | |
| 6-11 years; Serotype 3; Post-Inj. 2 | 337 (193 to 587) | 396 (162 to 967) | | |
| 6-11 years; Serotype 3; Post-Inj. 3 | 263 (164 to 424) | 390 (112 to 1358) | | |
| 6-11 years; Serotype 4; Pre-Inj. 1 | 32 (12.9 to 79.4) | 57.2 (19.2 to 170) | | |
| 6-11 years; Serotype 4; Post-Inj. 2 | 271 (152 to 484) | 285 (102 to 799) | | |
| 6-11 years; Serotype 4; Post-Inj. 3 | 270 (159 to 459) | 373 (121 to 1148) | | |
| 2-5 years; Serotype 1; Pre-Inj. 1 | 18.8 (6.79 to 52) | 7.08 (4.64 to 10.8) | | |
| 2-5 years; Serotype 1; Post-Inj. 2 | 44.2 (17.5 to 111) | 22.1 (6.38 to 76.7) | | |
| 2-5 years; Serotype 1; Post-Inj. 3 | 106 (52.3 to 213) | 55.5 (22.9 to 134) | | |
| 2-5 years; Serotype 2; Pre-Inj. 1 | 16.3 (7.95 to 33.6) | 17.4 (4.87 to 62) | | |
| 2-5 years; Serotype 2; Post-Inj. 2 | 123 (71.8 to 209) | 106 (18.5 to 604) | | |
| 2-5 years; Serotype 2; Post-Inj. 3 | 158 (107 to 234) | 412 (137 to 1233) | | |
| 2-5 years; Serotype 3; Pre-Inj. 1 | 26 (12.6 to 53.5) | 29.5 (9.15 to 95) | | |
| 2-5 years; Serotype 3; Post-Inj. 2 | 198 (136 to 288) | 265 (45.1 to 1563) | | |
| 2-5 years; Serotype 3; Post-Inj. 3 | 168 (132 to 215) | 1200 (512 to 2811) | | |
| 2-5 years; Serotype 4; Pre-Inj. 1 | 32.9 (13 to 83.4) | 20.7 (7.6 to 56.4) | | |
| 2-5 years; Serotype 4; Post-Inj. 2 | 210 (105 to 419) | 128 (34.3 to 482) | | |
| 2-5 years; Serotype 4; Post-Inj. 3 | 182 (85.1 to 389) | 298 (95.2 to 931) | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects with Antibody titer ≥ 10 (1/dil) Against Each Serotype with the Parental Dengue Virus Strains Post-injection 3 with ChimeriVax™ Dengue Tetravalent Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects with Antibody titer ≥ 10 (1/dil) Against Each Serotype with the Parental Dengue Virus Strains Post- |
|-----------------|---|

End point description:

Antibody titers against each serotype of the CYD dengue vaccine was assessed using the Dengue Plaque Reduction Neutralization Test (PRNT).

End point type Other pre-specified

End point timeframe:

Post-Inj. 3 and 1, 2, 3, 4, and 5 years Post-Inj. 3

| End point values | Group 1 | Group 2 | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 39 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| All subjects; Serotype 1; Post-Inj. 3 | 93.4 | 100 | | |
| All subjects; Serotype 1; 1 year Post-Inj. 3 | 75.8 | 81.8 | | |
| All subjects; Serotype 1; 2 years Post-Inj. 3 | 84.8 | 84.2 | | |
| All subjects; Serotype 1; 3 years Post-Inj. 3 | 75.9 | 67.6 | | |
| All subjects; Serotype 1; 4 years Post-Inj. 3 | 78.5 | 81.6 | | |
| All subjects; Serotype 1; 5 years Post-Inj. 3 | 76.6 | 83.3 | | |
| All subjects; Serotype 2; Post-Inj. 3 | 98.7 | 100 | | |
| All subjects; Serotype 2; 1 year Post-Inj. 3 | 91 | 88.2 | | |
| All subjects; Serotype 2; 2 years Post-Inj. 3 | 91.1 | 86.8 | | |
| All subjects; Serotype 2; 3 years Post-Inj. 3 | 86.1 | 83.8 | | |
| All subjects; Serotype 2; 4 years Post-Inj. 3 | 86.1 | 86.8 | | |
| All subjects; Serotype 2; 5 years Post-Inj. 3 | 81.8 | 88.9 | | |
| All subjects; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| All subjects; Serotype 3; 1 year Post-Inj. 3 | 96.7 | 96.8 | | |
| All subjects; Serotype 3; 2 years Post-Inj. 3 | 92.4 | 100 | | |
| All subjects; Serotype 3; 3 years Post-Inj. 3 | 93.7 | 91.9 | | |
| All subjects; Serotype 3; 4 years Post-Inj. 3 | 87.3 | 92.1 | | |
| All subjects; Serotype 3; 5 years Post-Inj. 3 | 85.7 | 88.9 | | |
| All subjects; Serotype 4; Post-Inj. 3 | 97.4 | 100 | | |
| All subjects; Serotype 4; 1 year Post-Inj. 3 | 95.3 | 93.3 | | |
| All subjects; Serotype 4; 2 years Post-Inj. 3 | 91.1 | 97.4 | | |
| All subjects; Serotype 4; 3 years Post-Inj. 3 | 89.9 | 89.2 | | |
| All subjects; Serotype 4; 4 years Post-Inj. 3 | 86.1 | 92.1 | | |

| | | | | |
|---|------|------|--|--|
| All subjects; Serotype 4; 5 years Post-Inj. 3 | 87 | 94.4 | | |
| 18-45 years; Serotype 1; Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 1; 1 year Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 1; 2 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 1; 3 years Post-Inj. 3 | 100 | 80 | | |
| 18-45 years; Serotype 1; 4 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 1; 5 years Post-Inj. 3 | 100 | 80 | | |
| 18-45 years; Serotype 2; Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 2; 1 year Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 2; 2 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 2; 3 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 2; 4 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 2; 5 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 3; 1 year Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 3; 2 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 3; 3 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 3; 4 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 3; 5 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 4; Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 4; 1 year Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 4; 2 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 4; 3 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 4; 4 years Post-Inj. 3 | 100 | 100 | | |
| 18-45 years; Serotype 4; 5 years Post-Inj. 3 | 100 | 100 | | |
| 12-17 years; Serotype 1; Post-Inj. 3 | 81.8 | 100 | | |
| 12-17 years; Serotype 1; 1 year Post-Inj. 3 | 65 | 88.9 | | |
| 12-17 years; Serotype 1; 2 years Post-Inj. 3 | 82.6 | 100 | | |
| 12-17 years; Serotype 1; 3 years Post-Inj. 3 | 82.6 | 80 | | |
| 12-17 years; Serotype 1; 4 years Post-Inj. 3 | 91.3 | 100 | | |
| 12-17 years; Serotype 1; 5 years Post-Inj. 3 | 90.9 | 100 | | |
| 12-17 years; Serotype 2; Post-Inj. 3 | 95.7 | 100 | | |
| 12-17 years; Serotype 2; 1 year Post-Inj. 3 | 90 | 100 | | |

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|--|------|------|--|--|
| 12-17 years; Serotype 2; 2 years Post-Inj. 3 | 91.3 | 90.9 | | |
| 12-17 years; Serotype 2; 3 years Post-Inj. 3 | 91.3 | 90 | | |
| 12-17 years; Serotype 2; 4 years Post-Inj. 3 | 91.3 | 100 | | |
| 12-17 years; Serotype 2; 5 years Post-Inj. 3 | 90.9 | 100 | | |
| 12-17 years; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| 12-17 years; Serotype 3; 1 year Post-Inj. 3 | 93.8 | 100 | | |
| 12-17 years; Serotype 3; 2 years Post-Inj. 3 | 95.7 | 100 | | |
| 12-17 years; Serotype 3; 3 years Post-Inj. 3 | 100 | 100 | | |
| 12-17 years; Serotype 3; 4 years Post-Inj. 3 | 91.3 | 100 | | |
| 12-17 years; Serotype 3; 5 years Post-Inj. 3 | 95.5 | 100 | | |
| 12-17 years; Serotype 4; Post-Inj. 3 | 100 | 100 | | |
| 12-17 years; Serotype 4; 1 year Post-Inj. 3 | 95 | 100 | | |
| 12-17 years; Serotype 4; 2 years Post-Inj. 3 | 87 | 100 | | |
| 12-17 years; Serotype 4; 3 years Post-Inj. 3 | 100 | 100 | | |
| 12-17 years; Serotype 4; 4 years Post-Inj. 3 | 95.7 | 100 | | |
| 12-17 years; Serotype 4; 5 years Post-Inj. 3 | 95.5 | 100 | | |
| 6-11 years; Serotype 1; Post-Inj. 3 | 100 | 100 | | |
| 6-11 years; Serotype 1; 1 year Post-Inj. 3 | 90 | 88.9 | | |
| 6-11 years; Serotype 1; 2 years Post-Inj. 3 | 79.2 | 81.8 | | |
| 6-11 years; Serotype 1; 3 years Post-Inj. 3 | 66.7 | 72.7 | | |
| 6-11 years; Serotype 1; 4 years Post-Inj. 3 | 66.7 | 81.8 | | |
| 6-11 years; Serotype 1; 5 years Post-Inj. 3 | 66.7 | 81.8 | | |
| 6-11 years; Serotype 2; Post-Inj. 3 | 100 | 100 | | |
| 6-11 years; Serotype 2; 1 year Post-Inj. 3 | 95 | 70 | | |
| 6-11 years; Serotype 2; 2 years Post-Inj. 3 | 87.5 | 72.7 | | |
| 6-11 years; Serotype 2; 3 years Post-Inj. 3 | 83.3 | 72.7 | | |
| 6-11 years; Serotype 2; 4 years Post-Inj. 3 | 83.3 | 81.8 | | |
| 6-11 years; Serotype 2; 5 years Post-Inj. 3 | 75 | 81.8 | | |
| 6-11 years; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| 6-11 years; Serotype 3; 1 year Post-Inj. 3 | 100 | 88.9 | | |
| 6-11 years; Serotype 3; 2 years Post-Inj. 3 | 83.3 | 100 | | |
| 6-11 years; Serotype 3; 3 years Post-Inj. 3 | 83.3 | 81.8 | | |
| 6-11 years; Serotype 3; 4 years Post-Inj. 3 | 75 | 81.8 | | |

| | | | | |
|---|------|------|--|--|
| 6-11 years; Serotype 3; 5 years Post-Inj. 3 | 83.3 | 90.9 | | |
| 6-11 years; Serotype 4; Post-Inj. 3 | 100 | 100 | | |
| 6-11 years; Serotype 4; 1 year Post-Inj. 3 | 100 | 100 | | |
| 6-11 years; Serotype 4; 2 years Post-Inj. 3 | 91.7 | 100 | | |
| 6-11 years; Serotype 4; 3 years Post-Inj. 3 | 87.5 | 81.8 | | |
| 6-11 years; Serotype 4; 4 years Post-Inj. 3 | 83.3 | 100 | | |
| 6-11 years; Serotype 4; 5 years Post-Inj. 3 | 83.3 | 90.9 | | |
| 2-5 years; Serotype 1; Post-Inj. 3 | 95.5 | 100 | | |
| 2-5 years; Serotype 1; 1 year Post-Inj. 3 | 61.1 | 63.6 | | |
| 2-5 years; Serotype 1; 2 years Post-Inj. 3 | 86.4 | 63.6 | | |
| 2-5 years; Serotype 1; 3 years Post-Inj. 3 | 68.2 | 45.5 | | |
| 2-5 years; Serotype 1; 4 years Post-Inj. 3 | 68.2 | 54.5 | | |
| 2-5 years; Serotype 1; 5 years Post-Inj. 3 | 63.6 | 72.7 | | |
| 2-5 years; Serotype 2; Post-Inj. 3 | 100 | 100 | | |
| 2-5 years; Serotype 2; 1 year Post-Inj. 3 | 84.2 | 87.5 | | |
| 2-5 years; Serotype 2; 2 years Post-Inj. 3 | 90.9 | 90.9 | | |
| 2-5 years; Serotype 2; 3 years Post-Inj. 3 | 77.3 | 81.8 | | |
| 2-5 years; Serotype 2; 4 years Post-Inj. 3 | 77.3 | 72.7 | | |
| 2-5 years; Serotype 2; 5 years Post-Inj. 3 | 72.7 | 81.8 | | |
| 2-5 years; Serotype 3; Post-Inj. 3 | 100 | 100 | | |
| 2-5 years; Serotype 3; 1 year Post-Inj. 3 | 94.7 | 100 | | |
| 2-5 years; Serotype 3; 2 years Post-Inj. 3 | 95.5 | 100 | | |
| 2-5 years; Serotype 3; 3 years Post-Inj. 3 | 95.5 | 90.9 | | |
| 2-5 years; Serotype 3; 4 years Post-Inj. 3 | 90.9 | 90.9 | | |
| 2-5 years; Serotype 3; 5 years Post-Inj. 3 | 72.7 | 72.7 | | |
| 2-5 years; Serotype 4; Post-Inj. 3 | 90.9 | 100 | | |
| 2-5 years; Serotype 4; 1 year Post-Inj. 3 | 88.9 | 75 | | |
| 2-5 years; Serotype 4; 2 years Post-Inj. 3 | 90.9 | 90.9 | | |
| 2-5 years; Serotype 4; 3 years Post-Inj. 3 | 77.3 | 81.8 | | |
| 2-5 years; Serotype 4; 4 years Post-Inj. 3 | 72.7 | 72.7 | | |
| 2-5 years; Serotype 4; 5 years Post-Inj. 3 | 77.3 | 90.9 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers (GMTs) of Antibodies Against Each Serotype with the Parental Dengue Virus Strain Post-injection 3 with ChimeriVax™ Dengue Tetravalent Vaccine

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|-----------------|---|
| End point title | Geometric Mean Titers (GMTs) of Antibodies Against Each Serotype with the Parental Dengue Virus Strain Post-injection 3 with ChimeriVax™ Dengue Tetravalent Vaccine |
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End point description:

Geometric mean titers against each serotype of the Parental Dengue Virus strains were assessed using the Dengue Plaque Reduction Neutralization Test (PRNT).

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| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Post-Inj. 3 and 1, 2, 3, 4, and 5 years Post-Inj. 3

| End point values | Group 1 | Group 2 | | |
|---|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 39 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| All subjects; Serotype 1; Post-Inj. 3 | 152 (98.4 to 235) | 279 (145 to 538) | | |
| All subjects; Serotype 1; 1 year Post-Inj. 3 | 79.8 (48 to 133) | 118 (54.8 to 256) | | |
| All subjects; Serotype 1; 2 years Post-Inj. 3 | 103 (65.8 to 161) | 151 (74.8 to 306) | | |
| All subjects; Serotype 1; 3 years Post-Inj. 3 | 75 (47.4 to 119) | 80.7 (36.4 to 179) | | |
| All subjects; Serotype 1; 4 years Post-Inj. 3 | 122 (75.4 to 197) | 148 (71.9 to 304) | | |
| All subjects; Serotype 1; 5 years Post-Inj. 3 | 93.5 (58.5 to 149) | 120 (56 to 255) | | |
| All subjects; Serotype 2; Post-Inj. 3 | 287 (207 to 398) | 461 (293 to 725) | | |
| All subjects; Serotype 2; 1 year Post-Inj. 3 | 189 (119 to 298) | 194 (106 to 355) | | |
| All subjects; Serotype 2; 2 years Post-Inj. 3 | 171 (115 to 254) | 182 (102 to 324) | | |
| All subjects; Serotype 2; 3 years Post-Inj. 3 | 168 (108 to 262) | 203 (104 to 397) | | |
| All subjects; Serotype 2; 4 years Post-Inj. 3 | 209 (133 to 330) | 264 (141 to 494) | | |
| All subjects; Serotype 2; 5 years Post-Inj. 3 | 150 (96.2 to 234) | 224 (119 to 420) | | |
| All subjects; Serotype 3; Post-Inj. 3 | 304 (240 to 385) | 674 (431 to 1052) | | |
| All subjects; Serotype 3; 1 year Post-Inj. 3 | 186 (125 to 275) | 241 (139 to 420) | | |
| All subjects; Serotype 3; 2 years Post-Inj. 3 | 182 (127 to 260) | 317 (194 to 518) | | |
| All subjects; Serotype 3; 3 years Post-Inj. 3 | 164 (113 to 238) | 179 (96.6 to 331) | | |

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|---|--------------------|---------------------|--|--|
| All subjects; Serotype 3; 4 years Post-Inj. 3 | 133 (89.4 to 198) | 167 (92 to 303) | | |
| All subjects; Serotype 3; 5 years Post-Inj. 3 | 130 (85.3 to 197) | 190 (102 to 354) | | |
| All subjects; Serotype 4; Post-Inj. 3 | 228 (171 to 303) | 330 (227 to 479) | | |
| All subjects; Serotype 4; 1 year Post-Inj. 3 | 158 (113 to 222) | 103 (57 to 187) | | |
| All subjects; Serotype 4; 2 years Post-Inj. 3 | 131 (94.3 to 182) | 142 (87.5 to 230) | | |
| All subjects; Serotype 4; 3 years Post-Inj. 3 | 161 (106 to 243) | 154 (83.6 to 283) | | |
| All subjects; Serotype 4; 4 years Post-Inj. 3 | 139 (92.2 to 210) | 163 (93.4 to 284) | | |
| All subjects; Serotype 4; 5 years Post-Inj. 3 | 99.3 (70.3 to 140) | 116 (67.4 to 201) | | |
| 18-45 years; Serotype 1; Post-Inj. 3 | 315 (183 to 543) | 599 (110 to 3273) | | |
| 18-45 years; Serotype 1; 1 year Post-Inj. 3 | 328 (183 to 589) | 779 (155 to 3906) | | |
| 18-45 years; Serotype 1; 2 years Post-Inj. 3 | 246 (165 to 366) | 535 (50.2 to 5690) | | |
| 18-45 years; Serotype 1; 3 years Post-Inj. 3 | 208 (148 to 292) | 408 (12.6 to 13196) | | |
| 18-45 years; Serotype 1; 4 years Post-Inj. 3 | 245 (155 to 387) | 484 (51.3 to 4573) | | |
| 18-45 years; Serotype 1; 5 years Post-Inj. 3 | 216 (125 to 375) | 294 (15.5 to 5588) | | |
| 18-45 years; Serotype 2; Post-Inj. 3 | 702 (431 to 1145) | 618 (366 to 1042) | | |
| 18-45 years; Serotype 2; 1 year Post-Inj. 3 | 474 (252 to 891) | 640 (294 to 1394) | | |
| 18-45 years; Serotype 2; 2 years Post-Inj. 3 | 410 (255 to 661) | 850 (167 to 4335) | | |
| 18-45 years; Serotype 2; 3 years Post-Inj. 3 | 427 (209 to 871) | 1132 (338 to 3793) | | |
| 18-45 years; Serotype 2; 4 years Post-Inj. 3 | 449 (221 to 912) | 855 (409 to 1791) | | |
| 18-45 years; Serotype 2; 5 years Post-Inj. 3 | 408 (225 to 739) | 957 (531 to 1724) | | |
| 18-45 years; Serotype 3; Post-Inj. 3 | 593 (347 to 1012) | 482 (253 to 920) | | |
| 18-45 years; Serotype 3; 1 year Post-Inj. 3 | 240 (163 to 352) | 394 (202 to 768) | | |
| 18-45 years; Serotype 3; 2 years Post-Inj. 3 | 306 (131 to 712) | 535 (215 to 1329) | | |
| 18-45 years; Serotype 3; 3 years Post-Inj. 3 | 549 (293 to 1029) | 542 (353 to 832) | | |
| 18-45 years; Serotype 3; 4 years Post-Inj. 3 | 402 (199 to 813) | 391 (214 to 713) | | |
| 18-45 years; Serotype 3; 5 years Post-Inj. 3 | 535 (233 to 1228) | 546 (361 to 826) | | |
| 18-45 years; Serotype 4; Post-Inj. 3 | 230 (110 to 481) | 533 (205 to 1390) | | |
| 18-45 years; Serotype 4; 1 year Post-Inj. 3 | 272 (111 to 666) | 257 (131 to 504) | | |
| 18-45 years; Serotype 4; 2 years Post-Inj. 3 | 217 (94.6 to 496) | 385 (205 to 726) | | |
| 18-45 years; Serotype 4; 3 years Post-Inj. 3 | 377 (152 to 940) | 615 (118 to 3213) | | |
| 18-45 years; Serotype 4; 4 years Post-Inj. 3 | 422 (221 to 806) | 491 (136 to 1772) | | |

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|--|---------------------|--------------------|--|--|
| 18-45 years; Serotype 4; 5 years Post-Inj. 3 | 194 (78.2 to 480) | 198 (59.9 to 652) | | |
| 12-17 years; Serotype 1; Post-Inj. 3 | 261 (81.3 to 840) | 504 (166 to 1534) | | |
| 12-17 years; Serotype 1; 1 year Post-Inj. 3 | 84 (26.4 to 267) | 183 (44.7 to 749) | | |
| 12-17 years; Serotype 1; 2 years Post-Inj. 3 | 168 (56 to 502) | 292 (100 to 853) | | |
| 12-17 years; Serotype 1; 3 years Post-Inj. 3 | 200 (68.5 to 586) | 109 (28 to 421) | | |
| 12-17 years; Serotype 1; 4 years Post-Inj. 3 | 428 (174 to 1057) | 453 (133 to 1540) | | |
| 12-17 years; Serotype 1; 5 years Post-Inj. 3 | 289 (117 to 717) | 182 (46.7 to 713) | | |
| 12-17 years; Serotype 2; Post-Inj. 3 | 427 (199 to 920) | 528 (220 to 1269) | | |
| 12-17 years; Serotype 2; 1 year Post-Inj. 3 | 235 (85.5 to 647) | 360 (142 to 912) | | |
| 12-17 years; Serotype 2; 2 years Post-Inj. 3 | 233 (104 to 525) | 231 (72.9 to 734) | | |
| 12-17 years; Serotype 2; 3 years Post-Inj. 3 | 297 (135 to 654) | 258 (72 to 927) | | |
| 12-17 years; Serotype 2; 4 years Post-Inj. 3 | 385 (177 to 839) | 894 (374 to 2134) | | |
| 12-17 years; Serotype 2; 5 years Post-Inj. 3 | 277 (141 to 546) | 508 (179 to 1438) | | |
| 12-17 years; Serotype 3; Post-Inj. 3 | 478 (294 to 778) | 827 (367 to 1864) | | |
| 12-17 years; Serotype 3; 1 year Post-Inj. 3 | 125 (52.8 to 297) | 454 (186 to 1108) | | |
| 12-17 years; Serotype 3; 2 years Post-Inj. 3 | 192 (104 to 352) | 341 (147 to 791) | | |
| 12-17 years; Serotype 3; 3 years Post-Inj. 3 | 279 (134 to 581) | 281 (105 to 755) | | |
| 12-17 years; Serotype 3; 4 years Post-Inj. 3 | 247 (122 to 499) | 526 (157 to 1763) | | |
| 12-17 years; Serotype 3; 5 years Post-Inj. 3 | 303 (158 to 580) | 395 (142 to 1100) | | |
| 12-17 years; Serotype 4; Post-Inj. 3 | 234 (161 to 340) | 241 (139 to 419) | | |
| 12-17 years; Serotype 4; 1 year Post-Inj. 3 | 188 (112 to 318) | 107 (39.2 to 291) | | |
| 12-17 years; Serotype 4; 2 years Post-Inj. 3 | 116 (62.4 to 214) | 126 (58.5 to 272) | | |
| 12-17 years; Serotype 4; 3 years Post-Inj. 3 | 401 (196 to 818) | 231 (82.7 to 645) | | |
| 12-17 years; Serotype 4; 4 years Post-Inj. 3 | 321 (155 to 663) | 509 (217 to 1197) | | |
| 12-17 years; Serotype 4; 5 years Post-Inj. 3 | 132 (80.6 to 216) | 100 (37.1 to 272) | | |
| 6-11 years; Serotype 1; Post-Inj. 3 | 101 (53.2 to 194) | 625 (116 to 3374) | | |
| 6-11 years; Serotype 1; 1 year Post-Inj. 3 | 104 (47.3 to 230) | 264 (37.2 to 1874) | | |
| 6-11 years; Serotype 1; 2 years Post-Inj. 3 | 67.5 (32.1 to 142) | 186 (35.2 to 977) | | |
| 6-11 years; Serotype 1; 3 years Post-Inj. 3 | 33.6 (16.9 to 66.6) | 81.6 (17.6 to 379) | | |
| 6-11 years; Serotype 1; 4 years Post-Inj. 3 | 51.6 (22.6 to 118) | 126 (27.6 to 572) | | |
| 6-11 years; Serotype 1; 5 years Post-Inj. 3 | 43.7 (19.6 to 97.5) | 129 (18.7 to 894) | | |

| | | | | |
|---|---------------------|--------------------|--|--|
| 6-11 years; Serotype 2; Post-Inj. 3 | 242 (127 to 459) | 364 (101 to 1304) | | |
| 6-11 years; Serotype 2; 1 year Post-Inj. 3 | 220 (91.7 to 528) | 92.2 (21.2 to 401) | | |
| 6-11 years; Serotype 2; 2 years Post-Inj. 3 | 154 (65.2 to 365) | 88.5 (24.9 to 315) | | |
| 6-11 years; Serotype 2; 3 years Post-Inj. 3 | 100 (45.2 to 222) | 101 (25.9 to 396) | | |
| 6-11 years; Serotype 2; 4 years Post-Inj. 3 | 132 (53.9 to 324) | 152 (44.9 to 512) | | |
| 6-11 years; Serotype 2; 5 years Post-Inj. 3 | 106 (41 to 276) | 134 (33.1 to 542) | | |
| 6-11 years; Serotype 3; Post-Inj. 3 | 263 (164 to 424) | 390 (112 to 1358) | | |
| 6-11 years; Serotype 3; 1 year Post-Inj. 3 | 349 (154 to 794) | 142 (34.4 to 590) | | |
| 6-11 years; Serotype 3; 2 years Post-Inj. 3 | 168 (70.4 to 401) | 244 (86.3 to 690) | | |
| 6-11 years; Serotype 3; 3 years Post-Inj. 3 | 95.3 (45.5 to 200) | 95.9 (29.1 to 316) | | |
| 6-11 years; Serotype 3; 4 years Post-Inj. 3 | 75.4 (33.4 to 171) | 83.2 (28.7 to 241) | | |
| 6-11 years; Serotype 3; 5 years Post-Inj. 3 | 88.8 (39.7 to 199) | 146 (37.2 to 572) | | |
| 6-11 years; Serotype 4; Post-Inj. 3 | 270 (159 to 459) | 373 (121 to 1148) | | |
| 6-11 years; Serotype 4; 1 year Post-Inj. 3 | 197 (105 to 372) | 159 (45.8 to 551) | | |
| 6-11 years; Serotype 4; 2 years Post-Inj. 3 | 133 (74.8 to 236) | 177 (53.1 to 590) | | |
| 6-11 years; Serotype 4; 3 years Post-Inj. 3 | 89.8 (47 to 172) | 139 (36.3 to 531) | | |
| 6-11 years; Serotype 4; 4 years Post-Inj. 3 | 79.3 (41.8 to 151) | 125 (55.1 to 285) | | |
| 6-11 years; Serotype 4; 5 years Post-Inj. 3 | 74.4 (38.2 to 145) | 115 (29.5 to 452) | | |
| 2-5 years; Serotype 1; Post-Inj. 3 | 106 (52.3 to 213) | 55.5 (22.9 to 134) | | |
| 2-5 years; Serotype 1; 1 year Post-Inj. 3 | 29.8 (10.9 to 81.9) | 21.7 (9.27 to 51) | | |
| 2-5 years; Serotype 1; 2 years Post-Inj. 3 | 66.1 (28.7 to 153) | 36 (10.7 to 121) | | |
| 2-5 years; Serotype 1; 3 years Post-Inj. 3 | 40.6 (17.9 to 92.4) | 29.1 (5.3 to 160) | | |
| 2-5 years; Serotype 1; 4 years Post-Inj. 3 | 60.9 (23.1 to 161) | 33.2 (9.39 to 117) | | |
| 2-5 years; Serotype 1; 5 years Post-Inj. 3 | 49.2 (19.5 to 124) | 52 (15.7 to 172) | | |
| 2-5 years; Serotype 2; Post-Inj. 3 | 158 (107 to 234) | 412 (137 to 1233) | | |
| 2-5 years; Serotype 2; 1 year Post-Inj. 3 | 86.4 (37.6 to 198) | 99 (23.5 to 417) | | |
| 2-5 years; Serotype 2; 2 years Post-Inj. 3 | 92.9 (47.3 to 182) | 145 (51.5 to 408) | | |
| 2-5 years; Serotype 2; 3 years Post-Inj. 3 | 107 (38.3 to 300) | 149 (33 to 674) | | |
| 2-5 years; Serotype 2; 4 years Post-Inj. 3 | 129 (46.2 to 361) | 79.2 (20.3 to 309) | | |
| 2-5 years; Serotype 2; 5 years Post-Inj. 3 | 78.5 (31.3 to 197) | 98.9 (28.1 to 348) | | |
| 2-5 years; Serotype 3; Post-Inj. 3 | 168 (132 to 215) | 1200 (512 to 2811) | | |

| | | | | |
|--|--------------------|--------------------|--|--|
| 2-5 years; Serotype 3; 1 year Post-Inj. 3 | 128 (61.2 to 266) | 154 (41.1 to 581) | | |
| 2-5 years; Serotype 3; 2 years Post-Inj. 3 | 148 (80.3 to 273) | 301 (79.9 to 1135) | | |
| 2-5 years; Serotype 3; 3 years Post-Inj. 3 | 98.8 (53.6 to 182) | 133 (25.7 to 692) | | |
| 2-5 years; Serotype 3; 4 years Post-Inj. 3 | 78.2 (37.6 to 163) | 72.2 (21.7 to 240) | | |
| 2-5 years; Serotype 3; 5 years Post-Inj. 3 | 47 (22.1 to 99.9) | 84.2 (20.8 to 342) | | |
| 2-5 years; Serotype 4; Post-Inj. 3 | 182 (85.1 to 389) | 298 (95.2 to 931) | | |
| 2-5 years; Serotype 4; 1 year Post-Inj. 3 | 82.4 (36.7 to 185) | 38.7 (7.86 to 191) | | |
| 2-5 years; Serotype 4; 2 years Post-Inj. 3 | 118 (53.4 to 259) | 81.1 (28.3 to 233) | | |
| 2-5 years; Serotype 4; 3 years Post-Inj. 3 | 78.9 (31.3 to 199) | 62.7 (18 to 218) | | |
| 2-5 years; Serotype 4; 4 years Post-Inj. 3 | 64.9 (25.6 to 164) | 40.8 (13.3 to 126) | | |
| 2-5 years; Serotype 4; 5 years Post-Inj. 3 | 78 (34.1 to 178) | 104 (32 to 338) | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Geometric Mean Titers (GMTs) of Antibodies Against Each Serotype with the Parental Dengue Virus Strain Before and Following Injection with ChimeriVax™ Dengue Tetravalent Vaccine in Adult Subjects

| | |
|------------------------|---|
| End point title | Geometric Mean Titers (GMTs) of Antibodies Against Each Serotype with the Parental Dengue Virus Strain Before and Following Injection with ChimeriVax™ Dengue Tetravalent Vaccine in Adult Subjects |
| End point description: | Geometric mean titers against each serotype of the Parental Dengue Virus strains were assessed using the microneutralization assay. |
| End point type | Other pre-specified |
| End point timeframe: | 1 and 2 years Post-Inj. 3 |

| End point values | Group 1 | Group 2 | | |
|--|------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 6 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1; 1 year Post-Inj. 3 | 206 (130 to 326) | 313 (85.8 to 1140) | | |
| Serotype 1; 2 years Post-Inj. 3 | 403 (272 to 597) | 562 (65.4 to 4830) | | |

| | | | | |
|---------------------------------|-------------------|-------------------|--|--|
| Serotype 2; 1 year Post-Inj. 3 | 176 (84.3 to 369) | 396 (146 to 1077) | | |
| Serotype 2; 2 years Post-Inj. 3 | 165 (72.5 to 373) | 450 (118 to 1714) | | |
| Serotype 3; 1 year Post-Inj. 3 | 342 (168 to 698) | 324 (188 to 558) | | |
| Serotype 3; 2 years Post-Inj. 3 | 502 (228 to 1105) | 581 (219 to 1538) | | |
| Serotype 4; 1 year Post-Inj. 3 | 168 (86 to 329) | 217 (98.6 to 480) | | |
| Serotype 4; 2 years Post-Inj. 3 | 116 (58.1 to 231) | 149 (47.5 to 467) | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects with Suspected Dengue Cases During the Four-Year Follow-Up Study Period

| | |
|-----------------|--|
| End point title | Number of Subjects with Suspected Dengue Cases During the Four-Year Follow-Up Study Period |
|-----------------|--|

End point description:

Dengue cases were assessed through the detection of febrile episodes, defined as temperature $\geq 38^{\circ}\text{C}$ for ≥ 48 hours. In the event of a febrile episode, blood was drawn during the acute phase (within 5 days of onset) and during the convalescent phase (within 7-14 days of onset) for laboratory testing to confirm the diagnosis of dengue infection. Virological diagnoses and confirmations were assessed using reverse transcriptase-polymerase chain reaction and serological diagnoses were assessed using an enzyme-linked immunosorbent assay.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

4 years post-Injection 3

| End point values | Group 1 | Group 2 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 81 | 39 | | |
| Units: Number of subjects | | | | |
| number (not applicable) | | | | |
| Follow-up Analysis Set | 81 | 39 | | |
| At least 1 suspected dengue case | 20 | 14 | | |
| At least 1 suspected dengue case; 18 to 45 years | 2 | 1 | | |
| At least 1 suspected dengue case; 12 to 17 years | 1 | 2 | | |
| At least 1 suspected dengue case; 6 to 11 years | 6 | 6 | | |
| At least 1 suspected dengue case; 2 to 5 years | 11 | 5 | | |
| At least 1 lab-confirmed dengue case | 3 | 3 | | |
| At least 1 lab-confirmed dengue case; 18 to 45 yrs | 0 | 0 | | |
| At least 1 lab-confirmed dengue case; 12 to 17 yrs | 0 | 1 | | |

| | | | | |
|---|---|---|--|--|
| At least 1 lab-confirmed dengue case; 6 to 11 yrs | 1 | 1 | | |
| At least 1 lab-confirmed dengue case; 2 to 5 yrs | 2 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse event data were collected from Day 0 (post-vaccination) up to 5 years Post-injection 3.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|-----|
| Dictionary version | 7.1 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Group 1 |
|-----------------------|---------|

Reporting group description:

Subjects received the CYD dengue vaccine for all three injections, one each on Days 0, 105, and 365, respectively.

| | |
|-----------------------|---------|
| Reporting group title | Group 2 |
|-----------------------|---------|

Reporting group description:

Subjects received typhoid vaccine (Typhim Vi) as first injection and CYD dengue vaccine as second and third injections 8 to 9 months apart (Days 105 and 365).

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events were collected during year 5.

| Serious adverse events | Group 1 | Group 2 | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 84 (2.38%) | 0 / 42 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Myofascial pain syndrome | | | |
| subjects affected / exposed | 1 / 84 (1.19%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Dengue fever | | | |
| subjects affected / exposed | 1 / 84 (1.19%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Group 1 | Group 2 | |
|---|----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 84 (0.00%) | 0 / 42 (0.00%) | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 25 November 2009 | The timeframe between two consecutive episodes of fever were defined for one and two episodes; Additional statistical analyses for safety, viremia, and immunogenicity were added; and the reporting period for pregnancies was revised. |
| 11 March 2011 | The use PRNT assay for study and all ongoing Dengue studies was confirmed. |
| 05 December 2011 | The follow up period for assessing the persistence of antibodies was extended to 5years. |
| 08 February 2012 | Effectuated minor changes received from the Institutional Review Board on protocol version 8.0 dated 05 December 2011. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/21477675>