



Clinical trial results: Immunogenicity and Large-Scale Safety of Tetravalent Dengue Vaccine in Healthy Subjects Aged 2 to 45 Years in Singapore

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2014-001713-26 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 14 October 2014 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 08 February 2016 |
| First version publication date | 17 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | CYD28 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00880893 |
| 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 | Director, Clinical Development, Sanofi Pasteur SA, 65 6431 2358, Anh.Wartel-Tram@sanofipasteur.com |
| Scientific contact | Director, Clinical Development, Sanofi Pasteur SA, 65 6431 2358, Anh.Wartel-Tram@sanofipasteur.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| 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? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

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|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 30 March 2015 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 14 October 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Safety and reactogenicity

Humoral immune response to dengue before and after each vaccination with CYD dengue vaccine

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:

Not applicable

| | |
|---|---------------|
| Actual start date of recruitment | 07 April 2009 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

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|--------------------------------------|-----------------|
| Country: Number of subjects enrolled | Singapore: 1198 |
| Worldwide total number of subjects | 1198 |
| 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) | 316 |
| Adolescents (12-17 years) | 187 |
| Adults (18-64 years) | 695 |

| | |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled from 07 April 2009 to 08 October 2009 at 5 clinical sites in Singapore.

Pre-assignment

Screening details:

A total of 1198 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, Monitor, Assessor |

Blinding implementation details:

An observer-design for the first vaccination and a single-blind design for the second and third vaccination were chosen to minimize the bias of the vaccine evaluation. The Investigator in charge of safety evaluation, the Sponsor, and the subjects/parents did not know which vaccine was administered at the first visit. For the second and third vaccinations, the subjects/parents did not know which vaccine was administered.

Arms

| | |
|------------------------------|--------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | CYD Dengue vaccine group |

Arm description:

Subjects received the CYD dengue vaccine at 0, 6, and 12 months as first, second, and third vaccinations, respectively.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | CYD Dengue vaccine |
| Investigational medicinal product code | 323 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5 mL, subcutaneous, 1 injection each at 0, 6, and 12 months.

| | |
|------------------|---------------|
| Arm title | Control group |
|------------------|---------------|

Arm description:

All subjects received a placebo at first vaccination (Month 0). Subjects <12 years received hepatitis A at second (Month 6) and third (Month 12) vaccinations. Subjects ≥12 years received influenza vaccine of Northern and Southern hemisphere formulations at second (Month 6) and third (Month 12) vaccinations.

| | |
|--|------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo (NaCl) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5 mL, subcutaneous, 1 injection at Month 0.

| | |
|--|---|
| Investigational medicinal product name | Hepatitis A vaccine (Havrix® pediatric formulation) |
| Investigational medicinal product code | |
| Other name | |

| | |
|---|---|
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 0.5 mL, intramuscular, subjects <12 years received hepatitis vaccine at second (Month 6) and third (Month 12) vaccinations. | |
| Investigational medicinal product name | Influenza vaccine (split virion, inactivated) Northern and Southern hemispheres year 2009-2010 formulations (Vaxigrip®) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL, intramuscular, subjects ≥12 years received 1 injection of the influenza vaccine of Northern and Southern hemisphere formulations at second (Month 6) and third (Month 12) vaccinations.

| Number of subjects in period 1 | CYD Dengue vaccine group | Control group |
|---------------------------------------|--------------------------|---------------|
| Started | 898 | 300 |
| Completed | 791 | 255 |
| Not completed | 107 | 45 |
| Consent withdrawn by subject | 15 | 11 |
| Serious adverse event | 3 | - |
| Lost to follow-up | 76 | 33 |
| Protocol deviation | 13 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | CYD Dengue vaccine group |
|-----------------------|--------------------------|

Reporting group description:

Subjects received the CYD dengue vaccine at 0, 6, and 12 months as first, second, and third vaccinations, respectively.

| | |
|-----------------------|---------------|
| Reporting group title | Control group |
|-----------------------|---------------|

Reporting group description:

All subjects received a placebo at first vaccination (Month 0). Subjects <12 years received hepatitis A at second (Month 6) and third (Month 12) vaccinations. Subjects ≥12 years received influenza vaccine of Northern and Southern hemisphere formulations at second (Month 6) and third (Month 12) vaccinations.

| Reporting group values | CYD Dengue vaccine group | Control group | Total |
|--|--------------------------|---------------|-------|
| Number of subjects | 898 | 300 | 1198 |
| 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) | 236 | 80 | 316 |
| Adolescents (12-17 years) | 141 | 46 | 187 |
| Adults (18-64 years) | 521 | 174 | 695 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 22.1 | 21.7 | |
| standard deviation | ± 11.97 | ± 11.76 | - |
| Gender categorical Units: Subjects | | | |
| Female | 471 | 139 | 610 |
| Male | 427 | 161 | 588 |

End points

End points reporting groups

| | |
|--|--------------------------|
| Reporting group title | CYD Dengue vaccine group |
| Reporting group description: | |
| Subjects received the CYD dengue vaccine at 0, 6, and 12 months as first, second, and third vaccinations, respectively. | |
| Reporting group title | Control group |
| Reporting group description: | |
| All subjects received a placebo at first vaccination (Month 0). Subjects <12 years received hepatitis A at second (Month 6) and third (Month 12) vaccinations. Subjects ≥12 years received influenza vaccine of Northern and Southern hemisphere formulations at second (Month 6) and third (Month 12) vaccinations. | |

Primary: Percentage of All Subjects Reporting Solicited Injection-site and Systemic Reactions Following Each Injection with CYD Dengue Tetravalent Vaccine

| | |
|---|--|
| End point title | Percentage of All Subjects Reporting Solicited Injection-site and Systemic Reactions Following Each Injection with CYD Dengue Tetravalent Vaccine ^[1] |
| End point description: | |
| Solicited injection site reactions: Pain, Erythema, and Swelling. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Asthenia. Grade 3 Solicited injection site reactions (2-11 years): Pain, Incapacitating, unable to perform usual activities; Erythema and Swelling, ≥5 cm. Grade 3 Solicited injection site reactions (adolescents and adults): Pain, Significant; prevents daily activity; Erythema and Swelling, >10 cm. Grade 3 Solicited systemic reactions: Fever, ≥39.0°C; Headache, Malaise, Myalgia, and Asthenia, Significant; prevents daily activity. | |
| End point type | Primary |
| End point timeframe: | |
| Day 0 up to Day 14 post-any and each injection | |

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 | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 898 | 300 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| Injection site Pain; Post-Any Injection | 53.9 | 66.7 | | |
| Grade 3 Injection site Pain; Post-Any Injection | 1 | 2 | | |
| Injection site Erythema; Post-Any Injection | 7.2 | 15.2 | | |
| Grade 3 Inj. site Erythema; Post-Any Inj. | 0 | 0 | | |
| Injection site Swelling; Post-Any Injection | 4.1 | 8.4 | | |
| Grade 3 Inj. site Swelling; Post-Any Inj. | 0 | 0 | | |
| Injection site Pain; Post-Injection 1 | 31.3 | 21.9 | | |
| Grade 3 Injection site Pain; Post-Injection 1 | 0.3 | 0.7 | | |
| Injection site Erythema; Post-Injection 1 | 2 | 2 | | |

| | | | | |
|---|------|------|--|--|
| Grade 3 Injection site Erythema; Post-Injection 1 | 0 | 0 | | |
| Injection site Swelling; Post-Injection 1 | 1.1 | 1.7 | | |
| Grade 3 Injection site Swelling; Post-Injection 1 | 0 | 0 | | |
| Injection site Pain; Post-Injection 2 | 36.9 | 54.4 | | |
| Grade 3 Injection site Pain; Post-Injection 2 | 0.5 | 0.7 | | |
| Injection site Erythema; Post-Injection 2 | 3.4 | 8.8 | | |
| Grade 3 Injection site Erythema; Post-Injection 2 | 0 | 0 | | |
| Injection site Swelling; Post-Injection 2 | 1.4 | 3.5 | | |
| Grade 3 Injection site Swelling; Post-Injection 2 | 0 | 0 | | |
| Injection site Pain; Post-Injection 3 | 34.9 | 50 | | |
| Grade 3 Injection site Pain; Post-Injection 3 | 0.2 | 0.7 | | |
| Injection site Erythema; Post-Injection 3 | 3.8 | 9.4 | | |
| Grade 3 Injection site Erythema; Post-Injection 3 | 0 | 0 | | |
| Injection site Swelling; Post-Injection 3 | 2.6 | 5.8 | | |
| Grade 3 Injection site Swelling; Post-Injection 3 | 0 | 0 | | |
| Fever; Post-Any Injection | 11.3 | 7.4 | | |
| Grade 3 Fever; Post-Any Injection | 1.9 | 1 | | |
| Headache; Post-Any Injection | 45.1 | 38.4 | | |
| Grade 3 Headache; Post-Any Injection | 3.8 | 2.7 | | |
| Malaise; Post-Any Injection | 41.8 | 35.4 | | |
| Grade 3 Malaise; Post-Any Injection | 4.3 | 2.7 | | |
| Myalgia; Post-Any Injection | 44.2 | 43.8 | | |
| Grade 3 Myalgia; Post-Any Injection | 2.6 | 2 | | |
| Asthenia; Post-Any Injection | 20.5 | 17.5 | | |
| Grade 3 Asthenia; Post-Any Injection | 1.3 | 0.7 | | |
| Fever; Post-Injection 1 | 4.6 | 2.7 | | |
| Grade 3 Fever; Post-Injection 1 | 0.6 | 0.7 | | |
| Headache; Post-Injection 1 | 30 | 27.3 | | |
| Grade 3 Headache; Post-Injection 1 | 2.4 | 1.3 | | |
| Malaise; Post-Injection 1 | 25 | 18.2 | | |
| Grade 3 Malaise; Post-Injection 1 | 2 | 0.7 | | |
| Myalgia; Post-Injection 1 | 29.4 | 19.2 | | |
| Grade 3 Myalgia; Post-Injection 1 | 1.3 | 1 | | |
| Asthenia; Post-Injection 1 | 12.8 | 6.1 | | |
| Grade 3 Asthenia; Post-Injection 1 | 0.7 | 0.3 | | |
| Fever; Post-Injection 2 | 3.3 | 2.8 | | |
| Grade 3 Fever; Post-Injection 2 | 0.6 | 0 | | |
| Headache; Post-Injection 2 | 22.8 | 21.8 | | |
| Grade 3 Headache; Post-Injection 2 | 0.7 | 1.1 | | |
| Malaise; Post-Injection 2 | 19.1 | 18.2 | | |
| Grade 3 Malaise; Post-Injection 2 | 1.2 | 1.1 | | |
| Myalgia; Post-Injection 2 | 24 | 29.5 | | |
| Grade 3 Myalgia; Post-Injection 2 | 0.9 | 0.7 | | |
| Asthenia; Post-Injection 2 | 9.3 | 10.2 | | |
| Grade 3 Asthenia; Post-Injection 2 | 0.3 | 0 | | |
| Fever; Post-Injection 3 | 4.8 | 2.9 | | |

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|------------------------------------|------|------|--|--|
| Grade 3 Fever; Post-Injection 3 | 0.8 | 0.4 | | |
| Headache; Post-Injection 3 | 20.1 | 19.8 | | |
| Grade 3 Headache; Post-Injection 3 | 1 | 0.4 | | |
| Malaise; Post-Injection 3 | 18.2 | 17.3 | | |
| Grade 3 Malaise; Post-Injection 3 | 1.4 | 1.1 | | |
| Myalgia; Post-Injection 3 | 21.8 | 26.3 | | |
| Grade 3 Myalgia; Post-Injection 3 | 0.5 | 0.7 | | |
| Asthenia; Post-Injection 3 | 8.5 | 9.4 | | |
| Grade 3 Asthenia; Post-Injection 3 | 0.4 | 0.4 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects By Age Group Reporting Solicited Injection-site and Systemic Reactions Following Each Injection with CYD Dengue Tetravalent Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects By Age Group Reporting Solicited Injection-site and Systemic Reactions Following Each Injection with CYD Dengue Tetravalent Vaccine ^[2] |
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End point description:

Solicited injection site reactions: Pain, Erythema, and Swelling. Solicited systemic reactions: Fever, Headache, Malaise, Myalgia, and Asthenia.

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| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 0 up to Day 14 post-each injection

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values | CYD Dengue vaccine group | Control group | | |
|--|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 898 | 300 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| 2-11 years; Injection site Pain, Post-Injection 1 | 33.9 | 30 | | |
| 2-11 years; Inj. site Erythema, Post-Inj. 1 | 6.4 | 7.5 | | |
| 2-11 years; Inj. site Swelling, Post-Inj. 1 | 3.8 | 6.3 | | |
| 12-17 years; Injection site Pain, Post-Injection 1 | 28.4 | 28.3 | | |
| 12-17 years; Inj. site Erythema, Post-Inj. 1 | 0 | 0 | | |
| 12-17 years; Inj. site Swelling, Post-Inj. 1 | 0 | 0 | | |
| 18-45 years; Injection site Pain, Post-Injection 1 | 30.9 | 16.4 | | |
| 18-45 years; Inj. site Erythema, Post-Inj. 1 | 0.6 | 0 | | |

| | | | | |
|--|------|------|--|--|
| 18-45 years; Inj. site Swelling, Post-Inj. 1 | 0.2 | 0 | | |
| 2-11 years; Injection site Pain, Post-Injection 2 | 38.3 | 42.1 | | |
| 2-11 years; Inj. site Erythema, Post-Inj. 2 | 9.4 | 5.3 | | |
| 2-11 years; Inj. site Swelling, Post-Inj. 2 | 4.7 | 3.9 | | |
| 12-17 years; Injection site Pain, Post-Injection 2 | 29.4 | 44.4 | | |
| 12-17 years; Inj. site Erythema, Post-Inj. 2 | 0 | 0 | | |
| 12-17 years; Inj. site Swelling, Post-Inj. 2 | 0 | 0 | | |
| 18-45 years; Injection site Pain, Post-Injection 2 | 38.3 | 62.8 | | |
| 18-45 years; Inj. site Erythema, Post-Inj. 2 | 1.4 | 12.8 | | |
| 18-45 years; Inj. site Swelling, Post-Inj. 2 | 0.2 | 4.3 | | |
| 2-11 years; Injection site Pain, Post-Injection 3 | 32.6 | 34.2 | | |
| 2-11 years; Inj. site Erythema, Post-Inj. 3 | 8.2 | 6.6 | | |
| 2-11 years; Inj. site Swelling, Post-Inj. 3 | 6.4 | 2.6 | | |
| 12-17 years; Injection site Pain, Post-Injection 3 | 26.7 | 38.6 | | |
| 12-17 years; Inj. site Erythema, Post-Inj. 3 | 0 | 0 | | |
| 12-17 years; Inj. site Swelling, Post-Inj. 3 | 0 | 0 | | |
| 18-45 years; Injection site Pain, Post-Injection 3 | 38.5 | 60.8 | | |
| 18-45 years; Inj. site Erythema, Post-Inj. 3 | 2.8 | 13.3 | | |
| 18-45 years; Inj. site Swelling, Post-Inj. 3 | 1.5 | 8.9 | | |
| 2-11 years; Fever, Post-Injection 1 | 8.1 | 6.3 | | |
| 2-11 years; Headache, Post-Injection 1 | 25 | 16.3 | | |
| 2-11 years; Malaise, Post-Injection 1 | 19.9 | 13.8 | | |
| 2-11 years; Myalgia, Post-Injection 1 | 23.7 | 16.3 | | |
| 2-11 years; Asthenia, Post-Injection 1 | 7.2 | 3.8 | | |
| 12-17 years; Fever, Post-Injection 1 | 7.1 | 2.2 | | |
| 12-17 years; Headache, Post-Injection 1 | 39.3 | 39.1 | | |
| 12-17 years; Malaise, Post-Injection 1 | 29.3 | 17.4 | | |
| 12-17 years; Myalgia, Post-Injection 1 | 32.1 | 23.9 | | |
| 12-17 years; Asthenia, Post-Injection 1 | 13.6 | 6.5 | | |
| 18-45 years; Fever, Post-Injection 1 | 2.3 | 1.2 | | |
| 18-45 years; Headache, Post-Injection 1 | 29.7 | 29.2 | | |
| 18-45 years; Malaise, Post-Injection 1 | 26.2 | 20.5 | | |
| 18-45 years; Myalgia, Post-Injection 1 | 31.3 | 19.3 | | |
| 18-45 years; Asthenia, Post-Injection 1 | 15.1 | 7 | | |
| 2-11 years; Fever, Post-Injection 2 | 6.8 | 6.6 | | |
| 2-11 years; Headache, Post-Injection 2 | 21.7 | 15.8 | | |
| 2-11 years; Malaise, Post-Injection 2 | 21.7 | 13.2 | | |
| 2-11 years; Myalgia, Post-Injection 2 | 24.7 | 22.4 | | |
| 2-11 years; Asthenia, Post-Injection 2 | 7.7 | 7.9 | | |

| | | | | |
|---|------|------|--|--|
| 12-17 years; Fever, Post-Injection 2 | 4.4 | 0 | | |
| 12-17 years; Headache, Post-Injection 2 | 19.9 | 22.2 | | |
| 12-17 years; Malaise, Post-Injection 2 | 16.2 | 20 | | |
| 12-17 years; Myalgia, Post-Injection 2 | 19.9 | 28.9 | | |
| 12-17 years; Asthenia, Post-Injection 2 | 8.8 | 6.7 | | |
| 18-45 years; Fever, Post-Injection 2 | 1.2 | 1.8 | | |
| 18-45 years; Headache, Post-Injection 2 | 24.2 | 24.4 | | |
| 18-45 years; Malaise, Post-Injection 2 | 18.6 | 20.1 | | |
| 18-45 years; Myalgia, Post-Injection 2 | 24.8 | 32.9 | | |
| 18-45 years; Asthenia, Post-Injection 2 | 10.2 | 12.2 | | |
| 2-11 years; Fever, Post-Injection 3 | 8.2 | 6.6 | | |
| 2-11 years; Headache, Post-Injection 3 | 17.6 | 11.8 | | |
| 2-11 years; Malaise, Post-Injection 3 | 18.5 | 14.5 | | |
| 2-11 years; Myalgia, Post-Injection 3 | 20.6 | 17.1 | | |
| 2-11 years; Asthenia, Post-Injection 3 | 7.7 | 3.9 | | |
| 12-17 years; Fever, Post-Injection 3 | 5.9 | 2.3 | | |
| 12-17 years; Headache, Post-Injection 3 | 20.7 | 20.5 | | |
| 12-17 years; Malaise, Post-Injection 3 | 18.5 | 18.2 | | |
| 12-17 years; Myalgia, Post-Injection 3 | 14.8 | 25 | | |
| 12-17 years; Asthenia, Post-Injection 3 | 5.9 | 11.4 | | |
| 18-45 years; Fever, Post-Injection 3 | 2.8 | 1.3 | | |
| 18-45 years; Headache, Post-Injection 3 | 21.2 | 23.4 | | |
| 18-45 years; Malaise, Post-Injection 3 | 17.9 | 18.4 | | |
| 18-45 years; Myalgia, Post-Injection 3 | 24.4 | 31 | | |
| 18-45 years; Asthenia, Post-Injection 3 | 9.6 | 11.4 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of All Subjects Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and After Each Vaccination With CYD Dengue Vaccine

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|-----------------|--|
| End point title | Percentage of All Subjects Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and After Each Vaccination With CYD Dengue Vaccine ^[3] |
|-----------------|--|

End point description:

Seropositivity against each dengue virus serotype was assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre-Injections 1, 2, and 3 and Post-Injections 1, 2, and 3

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 424 | 140 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Pre-Injection 1 | 14.6 | 17.1 | | |
| CYD dengue Serotype 1; Post-Injection 1 | 22.9 | 11.6 | | |
| CYD dengue Serotype 1; Pre-Injection 2 | 30.1 | 16.7 | | |
| CYD dengue Serotype 1; Post-Injection 2 | 54.9 | 18.3 | | |
| CYD dengue Serotype 1; Pre-Injection 3 | 45.8 | 13.8 | | |
| CYD dengue Serotype 1; Post-Injection 3 | 79.6 | 22 | | |
| CYD dengue Serotype 2; Pre-Injection 1 | 16.1 | 15 | | |
| CYD dengue Serotype 2; Post-Injection 1 | 39.5 | 10.1 | | |
| CYD dengue Serotype 2; Pre-Injection 2 | 39.3 | 16.7 | | |
| CYD dengue Serotype 2; Post-Injection 2 | 80.4 | 15 | | |
| CYD dengue Serotype 2; Pre-Injection 3 | 58.3 | 13.8 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 88.1 | 20.2 | | |
| CYD dengue Serotype 3; Pre-Injection 1 | 19.7 | 20.1 | | |
| CYD dengue Serotype 3; Post-Injection 1 | 58.7 | 21.7 | | |
| CYD dengue Serotype 3; Pre-Injection 2 | 63.9 | 31 | | |
| CYD dengue Serotype 3; Post-Injection 2 | 87.4 | 26.7 | | |
| CYD dengue Serotype 3; Pre-Injection 3 | 77.8 | 19 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 93.2 | 24.8 | | |
| CYD dengue Serotype 4; Pre-Injection 1 | 12.8 | 12.9 | | |
| CYD dengue Serotype 4; Post-Injection 1 | 67.3 | 11.6 | | |
| CYD dengue Serotype 4; Pre-Injection 2 | 69.1 | 16.7 | | |
| CYD dengue Serotype 4; Post-Injection 2 | 85.8 | 16.9 | | |
| CYD dengue Serotype 4; Pre-Injection 3 | 79.3 | 8.6 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 93.7 | 19.3 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects By Age Group Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Percentage of Subjects By Age Group Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine ^[4] |
|-----------------|--|

End point description:

Seropositivity against each dengue virus serotypes was assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre-Injection 1 and Post-Injection 3

Notes:

[4] - 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 | CYD Dengue vaccine group | Control group | | |
|--|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 148 | 47 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| 2-11 years, CYD dengue Serotype 1; Pre-Injection 1 | 4.7 | 8.5 | | |
| 2-11 years, CYD dengue Serotype 1; Post-Inj. 3 | 92.4 | 10.8 | | |
| 2-11 years, CYD dengue Serotype 2; Pre-Injection 1 | 5.4 | 2.1 | | |
| 2-11 years, CYD dengue Serotype 2; Post-Inj. 3 | 93.9 | 16.2 | | |
| 2-11 years, CYD dengue Serotype 3; Pre-Injection 1 | 11.6 | 10.6 | | |
| 2-11 years, CYD dengue Serotype 3; Post-Inj. 3 | 98.5 | 13.5 | | |
| 2-11 years, CYD dengue Serotype 4; Pre-Injection 1 | 6.8 | 6.4 | | |
| 2-11 years, CYD dengue Serotype 4; Post-Inj. 3 | 96.9 | 18.9 | | |
| 12-17 years, CYD dengue Serotype 1; Pre-Inj. 1 | 5.7 | 4.3 | | |
| 12-17 years, CYD dengue Serotype 1; Post-Inj. 3 | 68.3 | 13.2 | | |
| 12-17 years, CYD dengue Serotype 2; Pre-Inj. 1 | 10 | 4.3 | | |
| 12-17 years, CYD dengue Serotype 2; Post-Inj. 3 | 87 | 10.5 | | |
| 12-17 years, CYD dengue Serotype 3; Pre-Inj. 1 | 11.5 | 10.9 | | |
| 12-17 years, CYD dengue Serotype 3; Post-Inj. 3 | 88.5 | 21.1 | | |
| 12-17 years, CYD dengue Serotype 4; Pre-Inj. 1 | 6.5 | 2.2 | | |
| 12-17 years, CYD dengue Serotype 4; Post-Inj. 3 | 91.1 | 10.5 | | |
| 18-45 years, CYD dengue Serotype 1; Pre-Inj. 1 | 34.6 | 38.3 | | |
| 18-45 years, CYD dengue Serotype 1; Post-Inj. 3 | 76.5 | 44.1 | | |
| 18-45 years, CYD dengue Serotype 2; Pre-Inj. 1 | 34.1 | 38.3 | | |
| 18-45 years, CYD dengue Serotype 2; Post-Inj. 3 | 81.6 | 35.3 | | |
| 18-45 years, CYD dengue Serotype 3; Pre-Inj. 1 | 37 | 39.1 | | |

| | | | | |
|--|------|------|--|--|
| 18-45 years, CYD dengue Serotype 3; Post-Inj. 3 | 91.8 | 41.2 | | |
| 18-45 years, CYD dengue Serotype 4; Pre-Inj. 1 | 26.1 | 30.4 | | |
| 18-45 years, CYD dengue Serotype 4; Post-Inj. 3 | 92.8 | 29.4 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects By Age Group Who Achieved Seropositivity Against At least 1, 2, 3, or 4 of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Percentage of Subjects By Age Group Who Achieved Seropositivity Against At least 1, 2, 3, or 4 of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine ^[5] |
|-----------------|--|

End point description:

Seropositivity against at least 1, 2, 3, or 4 dengue virus serotypes was assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre-Injection 1 and Post-Injection 3

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values | CYD Dengue vaccine group | Control group | | |
|--|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 148 | 47 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| 2-11 yrs, CYD dengue ≥ 1 serotype; Pre-Inj. 1 | 19.6 | 27.7 | | |
| 2-11 yrs, CYD dengue ≥ 1 serotype; Post-Inj. 3 | 100 | 56.8 | | |
| 2-11 yrs, CYD dengue ≥ 2 serotypes; Pre-Inj. 1 | 6.1 | 0 | | |
| 2-11 yrs, CYD dengue ≥ 2 serotypes; Post-Inj. 3 | 99.2 | 2.7 | | |
| 2-11 yrs, CYD dengue ≥ 3 serotypes; Pre-Inj. 1 | 2 | 0 | | |
| 2-11 yrs, CYD dengue ≥ 3 serotypes; Post-Inj. 3 | 97 | 0 | | |
| 2-11 yrs, CYD dengue All 4 serotypes; Pre-Inj. 1 | 0.7 | 0 | | |
| 2-11 yrs, CYD dengue All 4 serotypes; Post-Inj. 3 | 84.8 | 0 | | |
| 12-17 yrs, CYD dengue ≥ 1 serotype; Pre-Inj. 1 | 13.6 | 15.2 | | |

| | | | | |
|--|------|------|--|--|
| 12-17 yrs, CYD dengue ≥ 1 serotype; Post-Inj. 3 | 98.4 | 26.3 | | |
| 12-17 yrs, CYD dengue ≥ 2 serotypes; Pre-Inj. 1 | 7.9 | 4.3 | | |
| 12-17 yrs, CYD dengue ≥ 2 serotypes; Post-Inj. 3 | 95.1 | 10.5 | | |
| 12-17 yrs, CYD dengue ≥ 3 serotypes; Pre-Inj. 1 | 7.1 | 2.2 | | |
| 12-17 yrs, CYD dengue ≥ 3 serotypes; Post-Inj. 3 | 81.3 | 10.5 | | |
| 12-17 yrs, CYD dengue All 4 serotypes; Pre-Inj. 1 | 5 | 0 | | |
| 12-17 yrs, CYD dengue All 4 serotypes; Post-Inj. 3 | 59.3 | 7.9 | | |
| 18-45 yrs, CYD dengue ≥ 1 serotype; Pre-Inj. 1 | 47.1 | 53.2 | | |
| 18-45 yrs, CYD dengue ≥ 1 serotype; Post-Inj. 3 | 100 | 55.9 | | |
| 18-45 yrs, CYD dengue ≥ 2 serotypes; Pre-Inj. 1 | 33.8 | 38.3 | | |
| 18-45 yrs, CYD dengue ≥ 2 serotypes; Post-Inj. 3 | 96.9 | 35.3 | | |
| 18-45 yrs, CYD dengue ≥ 3 serotypes; Pre-Inj. 1 | 27.9 | 31.9 | | |
| 18-45 yrs, CYD dengue ≥ 3 serotypes; Post-Inj. 3 | 83.7 | 32.4 | | |
| 18-45 yrs, CYD dengue All 4 serotypes; Pre-Inj. 1 | 22.1 | 21.3 | | |
| 18-45 yrs, CYD dengue All 4 serotypes; Post-Inj. 3 | 61.2 | 26.5 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of Antibodies In All Subjects Against Each Serotype with the Parental Dengue Virus Strain Before and Following Each Injection with CYD Dengue Vaccine

| | |
|-----------------|---|
| End point title | Geometric Mean Titers (GMTs) of Antibodies In All Subjects Against Each Serotype with the Parental Dengue Virus Strain Before and Following Each Injection with CYD Dengue Vaccine ^[6] |
|-----------------|---|

End point description:

Geometric mean titers against each serotype with the parental dengue virus strains were assessed using a dengue plaque reduction neutralization test (PRNT) assay.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre-Injections 1, 2, and 3 and Post-Injections 1, 2, and 3

Notes:

[6] - 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 | CYD Dengue vaccine group | Control group | | |
|--|--------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 424 | 140 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| CYD dengue Serotype 1; Pre-Injection 1 | 8.2 (7.2 to 9.33) | 8.23 (6.62 to 10.2) | | |
| CYD dengue Serotype 1; Post-Injection 1 | 10 (8.06 to 12.4) | 7.09 (5.48 to 9.18) | | |
| CYD dengue Serotype 1; Pre-Injection 2 | 12.9 (9.89 to 16.7) | 7.85 (5.79 to 10.6) | | |
| CYD dengue Serotype 1; Post-Injection 2 | 22.4 (17.1 to 29.3) | 7.91 (5.85 to 10.7) | | |
| CYD dengue Serotype 1; Pre-Injection 3 | 18 (14 to 23.2) | 7.4 (5.54 to 9.88) | | |
| CYD dengue Serotype 1; Post-Injection 3 | 46.6 (39 to 55.6) | 8.93 (7.08 to 11.3) | | |
| CYD dengue Serotype 2; Pre-Injection 1 | 9.06 (7.86 to 10.4) | 8.48 (6.69 to 10.8) | | |
| CYD dengue Serotype 2; Post-Injection 1 | 17.2 (13.3 to 22.2) | 7.39 (5.49 to 9.94) | | |
| CYD dengue Serotype 2; Pre-Injection 2 | 19.1 (14.3 to 25.5) | 9.79 (6.45 to 14.9) | | |
| CYD dengue Serotype 2; Post-Injection 2 | 50.3 (39 to 65) | 9.48 (6.22 to 14.4) | | |
| CYD dengue Serotype 2; Pre-Injection 3 | 24.4 (19.2 to 31.1) | 6.98 (5.38 to 9.07) | | |
| CYD dengue Serotype 2; Post-Injection 3 | 72.7 (61.6 to 85.8) | 8.88 (6.9 to 11.4) | | |
| CYD dengue Serotype 3; Pre-Injection 1 | 8.45 (7.54 to 9.47) | 8.93 (7.11 to 11.2) | | |
| CYD dengue Serotype 3; Post-Injection 1 | 28.2 (22 to 36.3) | 9.56 (6.72 to 13.6) | | |
| CYD dengue Serotype 3; Pre-Injection 2 | 29.7 (23.2 to 38) | 11.1 (7.6 to 16.3) | | |
| CYD dengue Serotype 3; Post-Injection 2 | 70.8 (56.8 to 88.2) | 10.5 (7.36 to 14.9) | | |
| CYD dengue Serotype 3; Pre-Injection 3 | 39.1 (31.2 to 48.9) | 8.23 (5.88 to 11.5) | | |
| CYD dengue Serotype 3; Post-Injection 3 | 100 (86.9 to 116) | 9.52 (7.41 to 12.2) | | |
| CYD dengue Serotype 4; Pre-Injection 1 | 6.93 (6.31 to 7.6) | 6.84 (5.86 to 7.99) | | |
| CYD dengue Serotype 4; Post-Injection 1 | 65.9 (49.1 to 88.3) | 6.31 (5.3 to 7.5) | | |
| CYD dengue Serotype 4; Pre-Injection 2 | 47.5 (36.5 to 61.8) | 7.91 (5.91 to 10.6) | | |
| CYD dengue Serotype 4; Post-Injection 2 | 90.2 (71.7 to 114) | 8 (5.89 to 10.9) | | |
| CYD dengue Serotype 4; Pre-Injection 3 | 47.1 (37.9 to 58.5) | 6.04 (5.09 to 7.17) | | |
| CYD dengue Serotype 4; Post-Injection 3 | 99.4 (87.4 to 113) | 7.66 (6.35 to 9.24) | | |

Statistical analyses

Primary: Geometric Mean Titers (GMTs) of Antibodies By Age Groups Against Each Serotype with the Parental Dengue Virus Strain Before and Following The Third Injection with CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Geometric Mean Titers (GMTs) of Antibodies By Age Groups Against Each Serotype with the Parental Dengue Virus Strain Before and Following The Third Injection with CYD Dengue Vaccine ^[7] |
|-----------------|--|

End point description:

Geometric mean titers against each dengue virus serotype were assessed using a dengue plaque reduction neutralization test (PRNT) assay.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre-Injection 1 and Post-Injection 3

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

| End point values | CYD Dengue vaccine group | Control group | | |
|--|--------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 148 | 47 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| 2-11 years, CYD dengue Serotype 1; Pre-Injection 1 | 5.33 (5.08 to 5.6) | 5.44 (5.01 to 5.92) | | |
| 2-11 years, CYD dengue Serotype 1; Post-Inj. 3 | 60.7 (49.5 to 74.3) | 6.32 (4.92 to 8.13) | | |
| 2-11 years, CYD dengue Serotype 2; Pre-Injection 1 | 5.85 (5.18 to 6.6) | 5.18 (4.82 to 5.57) | | |
| 2-11 years, CYD dengue Serotype 2; Post-Inj. 3 | 95.9 (76.7 to 120) | 6.09 (5.18 to 7.16) | | |
| 2-11 years, CYD dengue Serotype 3; Pre-Injection 1 | 6.24 (5.57 to 6.99) | 6.02 (5.04 to 7.17) | | |
| 2-11 years, CYD dengue Serotype 3; Post-Inj. 3 | 138 (115 to 165) | 6.67 (5.11 to 8.71) | | |
| 2-11 years, CYD dengue Serotype 4; Pre-Injection 1 | 5.64 (5.2 to 6.11) | 5.42 (4.92 to 5.97) | | |
| 2-11 years, CYD dengue Serotype 4; Post-Inj. 3 | 101 (84.6 to 122) | 6.92 (5.47 to 8.76) | | |
| 12-17 years, CYD dengue Serotype 1; Pre-Inj. 1 | 6.49 (5.31 to 7.92) | 5.47 (4.8 to 6.24) | | |
| 12-17 years, CYD dengue Serotype 1; Post-Inj. 3 | 28.9 (21.5 to 38.7) | 6.56 (5.14 to 8.37) | | |
| 12-17 years, CYD dengue Serotype 2; Pre-Inj. 1 | 7.47 (5.96 to 9.37) | 5.54 (4.69 to 6.56) | | |
| 12-17 years, CYD dengue Serotype 2; Post-Inj. 3 | 54 (41.1 to 70.9) | 6.35 (5.03 to 8) | | |
| 12-17 years, CYD dengue Serotype 3; Pre-Inj. 1 | 6.86 (5.82 to 8.09) | 6.83 (4.84 to 9.65) | | |
| 12-17 years, CYD dengue Serotype 3; Post-Inj. 3 | 74.1 (57.5 to 95.5) | 8.32 (5.57 to 12.4) | | |
| 12-17 years, CYD dengue Serotype 4; Pre-Inj. 1 | 5.83 (5.18 to 6.57) | 5.08 (4.92 to 5.23) | | |

| | | | | |
|---|---------------------|---------------------|--|--|
| 12-17 years, CYD dengue Serotype 4; Post-Inj. 3 | 80.4 (64.2 to 101) | 6.68 (4.87 to 9.15) | | |
| 18-45 years, CYD dengue Serotype 1; Pre-Inj. 1 | 16.7 (12.2 to 22.8) | 18.5 (10.4 to 32.9) | | |
| 18-45 years, CYD dengue Serotype 1; Post-Inj. 3 | 59.5 (38.7 to 91.6) | 18.3 (10.2 to 33) | | |
| 18-45 years, CYD dengue Serotype 2; Pre-Inj. 1 | 17.8 (12.8 to 24.7) | 21.1 (11.3 to 39.2) | | |
| 18-45 years, CYD dengue Serotype 2; Post-Inj. 3 | 72.7 (49.4 to 107) | 19.5 (9.69 to 39.1) | | |
| 18-45 years, CYD dengue Serotype 3; Pre-Inj. 1 | 14.6 (11.2 to 19) | 17.5 (10.2 to 30) | | |
| 18-45 years, CYD dengue Serotype 3; Post-Inj. 3 | 94.9 (69.4 to 130) | 16.3 (9.06 to 29.4) | | |
| 18-45 years, CYD dengue Serotype 4; Pre-Inj. 1 | 10.4 (8.22 to 13.2) | 11.7 (7.65 to 17.9) | | |
| 18-45 years, CYD dengue Serotype 4; Post-Inj. 3 | 127 (96 to 167) | 9.96 (6.47 to 15.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 2 to 11 Years Old Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects Aged 2 to 11 Years Old Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|---|

End point description:

Seropositivity against each dengue virus serotypes was assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil).

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

End point timeframe:

Pre-Injection 1, Post-Injection 3, and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 438 | 147 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Pre-Injection 1 | 4.7 | 8 | | |
| CYD dengue Serotype 1; Post-Injection 3 | 91 | 8.9 | | |
| CYD dengue Serotype 1; 1st year follow up | 41.8 | 6.8 | | |
| CYD dengue Serotype 1; 2nd year follow up | 27.1 | 0 | | |
| CYD dengue Serotype 1; 3rd year follow up | 16.5 | 0 | | |

| | | | | |
|---|------|------|--|--|
| CYD dengue Serotype 1; 4th year follow up | 9.6 | 0 | | |
| CYD dengue Serotype 2; Pre-Injection 1 | 5.4 | 2 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 94.4 | 13.3 | | |
| CYD dengue Serotype 2; 1st year follow up | 59.6 | 8.9 | | |
| CYD dengue Serotype 2; 2nd year follow up | 52.1 | 11.6 | | |
| CYD dengue Serotype 2; 3rd year follow up | 34.3 | 7 | | |
| CYD dengue Serotype 2; 4th year follow up | 36.9 | 2.4 | | |
| CYD dengue Serotype 3; Pre-Injection 1 | 11.6 | 10 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 97.9 | 13.6 | | |
| CYD dengue Serotype 3; 1st year follow up | 66 | 9.1 | | |
| CYD dengue Serotype 3; 2nd year follow up | 74.4 | 29.3 | | |
| CYD dengue Serotype 3; 3rd year follow up | 50 | 4.7 | | |
| CYD dengue Serotype 3; 4th year follow up | 37.7 | 2.4 | | |
| CYD dengue Serotype 4; Pre-Injection 1 | 6.8 | 6 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 97.2 | 20.5 | | |
| CYD dengue Serotype 4; 1st year follow up | 75.2 | 4.7 | | |
| CYD dengue Serotype 4; 2nd year follow up | 72.9 | 4.7 | | |
| CYD dengue Serotype 4; 3rd year follow up | 60.6 | 7 | | |
| CYD dengue Serotype 4; 4th year follow up | 49.3 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 12 to 17 Years Old Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Percentage of Subjects Aged 12 to 17 Years Old Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|--|

End point description:

Seropositivity against each dengue virus serotypes was assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil).

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

End point timeframe:

Pre-Injection 1, Post-Injection 3, and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 438 | 147 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Pre-Injection 1 | 5.7 | 4.3 | | |
| CYD dengue Serotype 1; Post-Injection 3 | 67.4 | 11.6 | | |
| CYD dengue Serotype 1; 1st year follow up | 25.8 | 7.3 | | |
| CYD dengue Serotype 1; 2nd year follow up | 19.5 | 7.5 | | |
| CYD dengue Serotype 1; 3rd year follow up | 16.1 | 5 | | |
| CYD dengue Serotype 1; 4th year follow up | 11.9 | 5.4 | | |
| CYD dengue Serotype 2; Pre-Injection 1 | 9.9 | 4.3 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 83.7 | 9.3 | | |
| CYD dengue Serotype 2; 1st year follow up | 44.3 | 4.9 | | |
| CYD dengue Serotype 2; 2nd year follow up | 52.3 | 10 | | |
| CYD dengue Serotype 2; 3rd year follow up | 35.5 | 5 | | |
| CYD dengue Serotype 2; 4th year follow up | 36.2 | 5.4 | | |
| CYD dengue Serotype 3; Pre-Injection 1 | 11.4 | 10.9 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 88.8 | 20.9 | | |
| CYD dengue Serotype 3; 1st year follow up | 61.7 | 5 | | |
| CYD dengue Serotype 3; 2nd year follow up | 56.3 | 12.5 | | |
| CYD dengue Serotype 3; 3rd year follow up | 48.8 | 5 | | |
| CYD dengue Serotype 3; 4th year follow up | 47.5 | 5.4 | | |
| CYD dengue Serotype 4; Pre-Injection 1 | 6.4 | 2.2 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 91.1 | 9.3 | | |
| CYD dengue Serotype 4; 1st year follow up | 73.5 | 2.4 | | |
| CYD dengue Serotype 4; 2nd year follow up | 71.1 | 10 | | |
| CYD dengue Serotype 4; 3rd year follow up | 66.7 | 5 | | |
| CYD dengue Serotype 4; 4th year follow up | 61 | 8.1 | | |

Statistical analyses

Secondary: Percentage of Subjects Aged 18 to 45 Years Old Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Percentage of Subjects Aged 18 to 45 Years Old Who Achieved Seropositivity Against Each of the Dengue Virus Serotypes Before and Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|--|

End point description:

Seropositivity against each dengue virus serotypes was assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil).

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

End point timeframe:

Pre-Injection 1, Post-Injection 3, and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 438 | 147 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Pre-Injection 1 | 33.1 | 38.8 | | |
| CYD dengue Serotype 1; Post-Injection 3 | 71.7 | 39.5 | | |
| CYD dengue Serotype 1; 1st year follow up | 45.9 | 31.8 | | |
| CYD dengue Serotype 1; 2nd year follow up | 43.6 | 34.1 | | |
| CYD dengue Serotype 1; 3rd year follow up | 40.4 | 30.8 | | |
| CYD dengue Serotype 1; 4th year follow up | 39.6 | 31.6 | | |
| CYD dengue Serotype 2; Pre-Injection 1 | 32.6 | 38.8 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 80.3 | 30.2 | | |
| CYD dengue Serotype 2; 1st year follow up | 66.4 | 40.9 | | |
| CYD dengue Serotype 2; 2nd year follow up | 68.4 | 34.1 | | |
| CYD dengue Serotype 2; 3rd year follow up | 55.3 | 35.9 | | |
| CYD dengue Serotype 2; 4th year follow up | 55.2 | 31.6 | | |
| CYD dengue Serotype 3; Pre-Injection 1 | 36.9 | 41.7 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 92.9 | 34.9 | | |
| CYD dengue Serotype 3; 1st year follow up | 68.6 | 38.6 | | |
| CYD dengue Serotype 3; 2nd year follow up | 77.8 | 46.3 | | |
| CYD dengue Serotype 3; 3rd year follow up | 67.9 | 35.9 | | |
| CYD dengue Serotype 3; 4th year follow up | 56.6 | 29.7 | | |

| | | | | |
|---|------|------|--|--|
| CYD dengue Serotype 4; Pre-Injection 1 | 25 | 31.3 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 93.7 | 32.6 | | |
| CYD dengue Serotype 4; 1st year follow up | 86.9 | 29.5 | | |
| CYD dengue Serotype 4; 2nd year follow up | 81.2 | 24.4 | | |
| CYD dengue Serotype 4; 3rd year follow up | 79.8 | 20.5 | | |
| CYD dengue Serotype 4; 4th year follow up | 77.6 | 21.1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 2 to 11 Years Old Who Achieved Seropositivity Against At least 1, 2, 3, or 4 of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects Aged 2 to 11 Years Old Who Achieved Seropositivity Against At least 1, 2, 3, or 4 of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|---|

End point description:

Seropositivity against at least 1, 2, 3, or 4 dengue virus serotypes was assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil).

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

End point timeframe:

Pre-Injection 1, Post-Injection 3, and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|--|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 438 | 147 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue ≥ 1 serotype; Pre-Injection 1 | 19.6 | 26 | | |
| CYD dengue ≥ 1 serotype; Post-Injection 3 | 100 | 51.1 | | |
| CYD dengue ≥ 1 serotype; 1st year follow up | 92.3 | 20 | | |
| CYD dengue ≥ 1 serotype; 2nd year follow up | 95 | 34.9 | | |
| CYD dengue ≥ 1 serotype; 3rd year follow up | 76.9 | 7 | | |
| CYD dengue ≥ 1 serotype; 4th year follow up | 72.1 | 4.8 | | |
| CYD dengue ≥ 2 serotypes; Pre-Injection 1 | 6.1 | 0 | | |
| CYD dengue ≥ 2 serotypes; Post-Injection 3 | 99.3 | 4.4 | | |

| | | | | |
|---|------|-----|--|--|
| CYD dengue ≥ 2 serotypes; 1st year follow up | 66.2 | 6.7 | | |
| CYD dengue ≥ 2 serotypes; 2nd year follow up | 70.7 | 9.3 | | |
| CYD dengue ≥ 2 serotypes; 3rd year follow up | 48.5 | 7 | | |
| CYD dengue ≥ 2 serotypes; 4th year follow up | 35.3 | 0 | | |
| CYD dengue ≥ 3 serotypes; Pre-Injection 1 | 2 | 0 | | |
| CYD dengue ≥ 3 serotypes; Post-Injection 3 | 96.5 | 0 | | |
| CYD dengue ≥ 3 serotypes; 1st year follow up | 52.8 | 2.2 | | |
| CYD dengue ≥ 3 serotypes; 2nd year follow up | 42.1 | 0 | | |
| CYD dengue ≥ 3 serotypes; 3rd year follow up | 23.9 | 4.7 | | |
| CYD dengue ≥ 3 serotypes; 4th year follow up | 16.2 | 0 | | |
| CYD dengue All 4 serotypes; Pre-Injection 1 | 0.7 | 0 | | |
| CYD dengue All 4 serotypes; Post-Injection 3 | 84 | 0 | | |
| CYD dengue All 4 serotypes; 1st year follow up | 29.6 | 0 | | |
| CYD dengue All 4 serotypes; 2nd year follow up | 15 | 0 | | |
| CYD dengue All 4 serotypes; 3rd year follow up | 11.2 | 0 | | |
| CYD dengue All 4 serotypes; 4th year follow up | 6.6 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 12 to 17 Years Old Who Achieved Seropositivity Against At least 1, 2, 3, or 4 of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Percentage of Subjects Aged 12 to 17 Years Old Who Achieved Seropositivity Against At least 1, 2, 3, or 4 of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|--|

End point description:

Seropositivity against at least 1, 2, 3, or 4 dengue virus serotypes was assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil).

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

End point timeframe:

Pre-Injection 1, Post-Injection 3, and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 438 | 147 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue ≥ 1 Serotype; Pre-Injection 1 | 13.5 | 15.2 | | |
| CYD dengue ≥ 1 Serotype; Post-Injection 3 | 97.8 | 25.6 | | |
| CYD dengue ≥ 1 Serotype; 1st year follow up | 94.7 | 7.3 | | |
| CYD dengue ≥ 1 Serotype; 2nd year follow up | 93 | 15 | | |
| CYD dengue ≥ 1 Serotype; 3rd year follow up | 89.5 | 5 | | |
| CYD dengue ≥ 1 serotype; 4th year follow up | 81.4 | 8.1 | | |
| CYD dengue ≥ 2 Serotypes; Pre-Injection 1 | 7.8 | 4.3 | | |
| CYD dengue ≥ 2 Serotypes; Post-Injection 3 | 94.8 | 9.3 | | |
| CYD dengue ≥ 2 Serotypes; 1st year follow up | 60.2 | 4.9 | | |
| CYD dengue ≥ 2 Serotypes; 2nd year follow up | 62.5 | 10 | | |
| CYD dengue ≥ 2 Serotypes; 3rd year follow up | 45.2 | 5 | | |
| CYD dengue ≥ 2 serotypes; 4th year follow up | 44.9 | 5.4 | | |
| CYD dengue ≥ 3 Serotypes; Pre-Injection 1 | 7.1 | 2.2 | | |
| CYD dengue ≥ 3 Serotypes; Post-Injection 3 | 80.7 | 9.3 | | |
| CYD dengue ≥ 3 Serotypes; 1st year follow up | 33.1 | 4.9 | | |
| CYD dengue ≥ 3 Serotypes; 2nd year follow up | 31.3 | 7.5 | | |
| CYD dengue ≥ 3 Serotypes; 3rd year follow up | 22.6 | 5 | | |
| CYD dengue ≥ 3 serotypes; 4th year follow up | 20.3 | 5.4 | | |
| CYD dengue All 4 Serotypes; Pre-Injection 1 | 5 | 0 | | |
| CYD dengue All 4 Serotypes; Post-Injection 3 | 57 | 7 | | |
| CYD dengue All 4 Serotypes; 1st year follow up | 15.8 | 2.4 | | |
| CYD dengue All 4 Serotypes; 2nd year follow up | 11.7 | 7.5 | | |
| CYD dengue All 4 Serotypes; 3rd year follow up | 8.9 | 5 | | |
| CYD dengue All 4 serotypes; 4th year follow up | 9.3 | 5.4 | | |

Statistical analyses

Secondary: Percentage of Subjects Aged 18 to 45 Years Old Who Achieved Seropositivity Against At least 1, 2, 3, or 4 of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Percentage of Subjects Aged 18 to 45 Years Old Who Achieved Seropositivity Against At least 1, 2, 3, or 4 of the Dengue Virus Serotypes Before and After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|--|

End point description:

Seropositivity against at least 1, 2, 3, or 4 dengue virus serotypes was assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil).

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

End point timeframe:

Pre-Injection 1, Post-Injection 3, and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 438 | 147 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue ≥ 1 Serotype; Pre-Injection 1 | 46.5 | 55.1 | | |
| CYD dengue ≥ 1 Serotype; Post-Injection 3 | 100 | 53.5 | | |
| CYD dengue ≥ 1 Serotype; 1st year follow up | 96.7 | 50 | | |
| CYD dengue ≥ 1 Serotype; 2nd year follow up | 96.6 | 56.1 | | |
| CYD dengue ≥ 1 Serotype; 3rd year follow up | 93 | 41 | | |
| CYD dengue ≥ 1 serotype; 4th year follow up | 92.5 | 36.8 | | |
| CYD dengue ≥ 2 Serotypes; Pre-Injection 1 | 32.4 | 38.8 | | |
| CYD dengue ≥ 2 Serotypes; Post-Injection 3 | 97.6 | 32.6 | | |
| CYD dengue ≥ 2 Serotypes; 1st year follow up | 73.8 | 38.6 | | |
| CYD dengue ≥ 2 Serotypes; 2nd year follow up | 76.9 | 34.1 | | |
| CYD dengue ≥ 2 Serotypes; 3rd year follow up | 63.2 | 33.3 | | |
| CYD dengue ≥ 2 serotypes; 4th year follow up | 54.2 | 28.9 | | |
| CYD dengue ≥ 3 Serotypes; Pre-Injection 1 | 26.8 | 32.7 | | |
| CYD dengue ≥ 3 Serotypes; Post-Injection 3 | 83.5 | 27.9 | | |
| CYD dengue ≥ 3 Serotypes; 1st year follow up | 55.7 | 34.1 | | |
| CYD dengue ≥ 3 Serotypes; 2nd year follow up | 56.4 | 29.3 | | |

| | | | | |
|---|------|------|--|--|
| CYD dengue ≥ 3 Serotypes; 3rd year follow up | 46.5 | 30.8 | | |
| CYD dengue ≥ 3 serotypes; 4th year follow up | 43 | 26.3 | | |
| CYD dengue All 4 Serotypes; Pre-Injection 1 | 21.1 | 22.4 | | |
| CYD dengue All 4 Serotypes; Post-Injection 3 | 56.7 | 23.3 | | |
| CYD dengue All 4 Serotypes; 1st year follow up | 41 | 18.2 | | |
| CYD dengue All 4 Serotypes; 2nd year follow up | 41 | 19.5 | | |
| CYD dengue All 4 Serotypes; 3rd year follow up | 39.5 | 17.9 | | |
| CYD dengue All 4 serotypes; 4th year follow up | 37.4 | 21.1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies In Subjects 2 to 11 Years Old Against Each Serotype with the Parental Dengue Virus Strain Before and Following The Third Injection with CYD Dengue Vaccine

| | |
|-----------------|---|
| End point title | Geometric Mean Titers (GMTs) of Antibodies In Subjects 2 to 11 Years Old Against Each Serotype with the Parental Dengue Virus Strain Before and Following The Third Injection with CYD Dengue Vaccine |
|-----------------|---|

End point description:

Geometric mean titers against each serotype with the dengue virus strain were assessed using a dengue plaque reduction neutralization test (PRNT) assay.

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

End point timeframe:

Pre-Injection 1, Post-Injection 3, and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 438 | 147 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| CYD dengue Serotype 1; Pre-Injection 1 | 5.33 (5.08 to 5.6) | 5.42 (5 to 5.86) | | |
| CYD dengue Serotype 1; Post-Injection 3 | 56.6 (46.5 to 68.9) | 6.06 (4.93 to 7.46) | | |
| CYD dengue Serotype 1; 1st year follow up | 12.1 (9.92 to 14.7) | 5.52 (4.92 to 6.19) | | |
| CYD dengue Serotype 1; 2nd year follow up | 8.89 (7.5 to 10.5) | 5 (5 to 5) | | |
| CYD dengue Serotype 1; 3rd year follow up | 7.35 (6.22 to 8.67) | 5 (5 to 5) | | |

| | | | | |
|---|---------------------|---------------------|--|--|
| CYD dengue Serotype 1; 4th year follow up | 6.21 (5.51 to 7) | 5 (5 to 5) | | |
| CYD dengue Serotype 2; Pre-Injection 1 | 5.85 (5.18 to 6.6) | 5.17 (4.83 to 5.53) | | |
| CYD dengue Serotype 2; Post-Injection 3 | 101 (81.7 to 125) | 5.88 (5.15 to 6.72) | | |
| CYD dengue Serotype 2; 1st year follow up | 21.1 (16.6 to 26.9) | 5.86 (4.79 to 7.16) | | |
| CYD dengue Serotype 2; 2nd year follow up | 16.4 (12.9 to 20.9) | 6.11 (5.1 to 7.32) | | |
| CYD dengue Serotype 2; 3rd year follow up | 11.7 (9.1 to 15.1) | 5.58 (4.86 to 6.41) | | |
| CYD dengue Serotype 2; 4th year follow up | 14.2 (10.7 to 19) | 5.11 (4.89 to 5.32) | | |
| CYD dengue Serotype 3; Pre-Injection 1 | 6.24 (5.57 to 6.99) | 5.95 (5.04 to 7.02) | | |
| CYD dengue Serotype 3; Post-Injection 3 | 136 (114 to 162) | 6.54 (5.2 to 8.22) | | |
| CYD dengue Serotype 3; 1st year follow up | 25.4 (20.1 to 32.1) | 5.87 (5 to 6.89) | | |
| CYD dengue Serotype 3; 2nd year follow up | 29.9 (23.4 to 38.1) | 10.1 (6.68 to 15.2) | | |
| CYD dengue Serotype 3; 3rd year follow up | 14.6 (11.7 to 18.3) | 5.43 (4.83 to 6.1) | | |
| CYD dengue Serotype 3; 4th year follow up | 11.4 (9.22 to 14.1) | 5.09 (4.91 to 5.29) | | |
| CYD dengue Serotype 4; Pre-Injection 1 | 5.64 (5.2 to 6.11) | 5.39 (4.92 to 5.91) | | |
| CYD dengue Serotype 4; Post-Injection 3 | 104 (87.2 to 125) | 7.2 (5.74 to 9.05) | | |
| CYD dengue Serotype 4; 1st year follow up | 31.8 (25.6 to 39.6) | 5.69 (4.7 to 6.89) | | |
| CYD dengue Serotype 4; 2nd year follow up | 30.6 (24.2 to 38.6) | 5.68 (4.74 to 6.82) | | |
| CYD dengue Serotype 4; 3rd year follow up | 22.3 (17.5 to 28.5) | 6.31 (4.84 to 8.24) | | |
| CYD dengue Serotype 4; 4th year follow up | 16.5 (13.1 to 20.7) | 5 (5 to 5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies In Subjects 12 to 17 Years Old Against Each Serotype with the Parental Dengue Virus Strain Before and Following The Third Injection with CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Geometric Mean Titers (GMTs) of Antibodies In Subjects 12 to 17 Years Old Against Each Serotype with the Parental Dengue Virus Strain Before and Following The Third Injection with CYD Dengue Vaccine |
|-----------------|--|

End point description:

Geometric mean titers against each serotype with the dengue virus strain were assessed using a dengue plaque reduction neutralization test (PRNT) assay.

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

End point timeframe:

Pre-Injection 1, Post-Injection 3, and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 438 | 147 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| CYD dengue Serotype 1; Pre-Injection 1 | 6.47 (5.31 to 7.89) | 5.47 (4.8 to 6.24) | | |
| CYD dengue Serotype 1; Post-Injection 3 | 28.5 (21.4 to 37.9) | 6.36 (5.12 to 7.89) | | |
| CYD dengue Serotype 1; 1st year follow up | 9.69 (7.53 to 12.5) | 5.69 (4.88 to 6.63) | | |
| CYD dengue Serotype 1; 2nd year follow up | 8.31 (6.58 to 10.5) | 5.91 (4.8 to 7.27) | | |
| CYD dengue Serotype 1; 3rd year follow up | 8.02 (6.3 to 10.2) | 5.54 (4.79 to 6.39) | | |
| CYD dengue Serotype 1; 4th year follow up | 7.41 (5.85 to 9.38) | 5.51 (4.8 to 6.34) | | |
| CYD dengue Serotype 2; Pre-Injection 1 | 7.45 (5.95 to 9.33) | 5.54 (4.69 to 6.56) | | |
| CYD dengue Serotype 2; Post-Injection 3 | 48.7 (37.4 to 63.5) | 6.17 (5.03 to 7.58) | | |
| CYD dengue Serotype 2; 1st year follow up | 16.6 (12.4 to 22.1) | 5.58 (4.78 to 6.52) | | |
| CYD dengue Serotype 2; 2nd year follow up | 18.7 (14.1 to 24.7) | 6.38 (4.92 to 8.27) | | |
| CYD dengue Serotype 2; 3rd year follow up | 13.3 (10.1 to 17.6) | 5.77 (4.71 to 7.07) | | |
| CYD dengue Serotype 2; 4th year follow up | 14 (10.4 to 18.8) | 5.8 (4.68 to 7.17) | | |
| CYD dengue Serotype 3; Pre-Injection 1 | 6.84 (5.81 to 8.06) | 6.83 (4.84 to 9.65) | | |
| CYD dengue Serotype 3; Post-Injection 3 | 71.4 (56.3 to 90.7) | 8.1 (5.66 to 11.6) | | |
| CYD dengue Serotype 3; 1st year follow up | 19.7 (15.1 to 25.6) | 6.27 (4.55 to 8.64) | | |
| CYD dengue Serotype 3; 2nd year follow up | 20.5 (15.6 to 27.1) | 7.54 (5.16 to 11) | | |
| CYD dengue Serotype 3; 3rd year follow up | 15.3 (11.8 to 19.9) | 6.17 (4.58 to 8.31) | | |
| CYD dengue Serotype 3; 4th year follow up | 13.7 (10.7 to 17.6) | 6.47 (4.49 to 9.3) | | |
| CYD dengue Serotype 4; Pre-Injection 1 | 5.83 (5.17 to 6.56) | 5.08 (4.92 to 5.23) | | |
| CYD dengue Serotype 4; Post-Injection 3 | 79.2 (64.2 to 97.8) | 6.45 (4.89 to 8.53) | | |
| CYD dengue Serotype 4; 1st year follow up | 30.8 (24.3 to 39) | 5.17 (4.84 to 5.52) | | |
| CYD dengue Serotype 4; 2nd year follow up | 33.4 (25.6 to 43.6) | 6.18 (4.99 to 7.65) | | |
| CYD dengue Serotype 4; 3rd year follow up | 23.1 (18.3 to 29.2) | 5.55 (4.79 to 6.42) | | |
| CYD dengue Serotype 4; 4th year follow up | 20.8 (16.2 to 26.6) | 5.43 (4.92 to 6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 2 to 11 Years Immune at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Percentage of Subjects Aged 2 to 11 Years Immune at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|--|

End point description:

Geometric mean titers against each serotype with the dengue virus strain were assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil). Dengue subjects immune at baseline are defined as those subjects with titers ≥ 10 (1/dil) against at least one dengue serotype at baseline.

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

End point timeframe:

Post-Injection 3 and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 114 | 47 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Post-Injection 3 | 96.3 | 0 | | |
| CYD dengue Serotype 1; 1st year follow up | 74.1 | 7.7 | | |
| CYD dengue Serotype 1; 2nd year follow up | 55.6 | 0 | | |
| CYD dengue Serotype 1; 3rd year follow up | 33.3 | 0 | | |
| CYD dengue Serotype 1; 4th year follow up | 22.2 | 0 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 100 | 15.4 | | |
| CYD dengue Serotype 2; 1st year follow up | 85.2 | 15.4 | | |
| CYD dengue Serotype 2; 2nd year follow up | 66.7 | 16.7 | | |
| CYD dengue Serotype 2; 3rd year follow up | 48.1 | 16.7 | | |
| CYD dengue Serotype 2; 4th year follow up | 48.1 | 0 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 100 | 23.1 | | |

| | | | | |
|---|------|------|--|--|
| CYD dengue Serotype 3; 1st year follow up | 88.9 | 7.7 | | |
| CYD dengue Serotype 3; 2nd year follow up | 81.5 | 16.7 | | |
| CYD dengue Serotype 3; 3rd year follow up | 59.3 | 8.3 | | |
| CYD dengue Serotype 3; 4th year follow up | 50 | 0 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 100 | 23.1 | | |
| CYD dengue Serotype 4; 1st year follow up | 88.9 | 15.4 | | |
| CYD dengue Serotype 4; 2nd year follow up | 74.1 | 0 | | |
| CYD dengue Serotype 4; 3rd year follow up | 70.4 | 16.7 | | |
| CYD dengue Serotype 4; 4th year follow up | 70.4 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 2 to 11 Years Naïve at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects Aged 2 to 11 Years Naïve at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|---|

End point description:

Geometric mean titers against each serotype with the dengue virus strain were assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil). Dengue subjects naïve at baseline are defined as those subjects with titers < 10 (1/dil) against all dengue serotypes at baseline.

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

End point timeframe:

Post-Injection 3 and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 313 | 98 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Post-Injection 3 | 89.6 | 12.5 | | |
| CYD dengue Serotype 1; 1st year follow up | 33.6 | 6.5 | | |
| CYD dengue Serotype 1; 2nd year follow up | 20.5 | 0 | | |
| CYD dengue Serotype 1; 3rd year follow up | 12.4 | 0 | | |

| | | | | |
|---|------|------|--|--|
| CYD dengue Serotype 1; 4th year follow up | 6.5 | 0 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 93 | 12.5 | | |
| CYD dengue Serotype 2; 1st year follow up | 54 | 6.3 | | |
| CYD dengue Serotype 2; 2nd year follow up | 49.1 | 9.7 | | |
| CYD dengue Serotype 2; 3rd year follow up | 31.1 | 3.2 | | |
| CYD dengue Serotype 2; 4th year follow up | 34.3 | 3.3 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 97.4 | 9.7 | | |
| CYD dengue Serotype 3; 1st year follow up | 60.2 | 9.7 | | |
| CYD dengue Serotype 3; 2nd year follow up | 72.4 | 34.5 | | |
| CYD dengue Serotype 3; 3rd year follow up | 47.2 | 3.2 | | |
| CYD dengue Serotype 3; 4th year follow up | 34.3 | 3.3 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 96.5 | 19.4 | | |
| CYD dengue Serotype 4; 1st year follow up | 71.7 | 0 | | |
| CYD dengue Serotype 4; 2nd year follow up | 73.2 | 6.5 | | |
| CYD dengue Serotype 4; 3rd year follow up | 58.7 | 3.2 | | |
| CYD dengue Serotype 4; 4th year follow up | 44.4 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 12 to 17 Years Immune at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects Aged 12 to 17 Years Immune at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|---|

End point description:

Geometric mean titers against each serotype with the dengue virus strain were assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil). Dengue subjects immune at baseline are defined as those subjects with titers ≥ 10 (1/dil) against at least one dengue serotype at baseline.

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

End point timeframe:

Post-Injection 3 and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|--|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 114 | 47 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Post-Injection 3 | 94.4 | 33.3 | | |
| CYD dengue Serotype 1; 1st year follow up | 58.8 | 20 | | |
| CYD dengue Serotype 1; 2nd year follow up | 46.7 | 16.7 | | |
| CYD dengue Serotype 1; 3rd year follow up | 43.8 | 16.7 | | |
| CYD dengue Serotype 1; 4th year follow up | 42.9 | 20 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 94.4 | 16.7 | | |
| CYD dengue Serotype 2; 1st year follow up | 82.4 | 20 | | |
| CYD dengue Serotype 2; 2nd year follow up | 73.3 | 33.3 | | |
| CYD dengue Serotype 2; 3rd year follow up | 68.8 | 16.7 | | |
| CYD dengue Serotype 2; 4th year follow up | 71.4 | 20 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 100 | 50 | | |
| CYD dengue Serotype 3; 1st year follow up | 76.5 | 20 | | |
| CYD dengue Serotype 3; 2nd year follow up | 80 | 50 | | |
| CYD dengue Serotype 3; 3rd year follow up | 68.8 | 16.7 | | |
| CYD dengue Serotype 3; 4th year follow up | 71.4 | 20 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 100 | 33.3 | | |
| CYD dengue Serotype 4; 1st year follow up | 100 | 20 | | |
| CYD dengue Serotype 4; 2nd year follow up | 100 | 16.7 | | |
| CYD dengue Serotype 4; 3rd year follow up | 93.8 | 16.7 | | |
| CYD dengue Serotype 4; 4th year follow up | 100 | 20 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 12 to 17 Years Naïve at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Percentage of Subjects Aged 12 to 17 Years Naïve at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue |
|-----------------|--|

End point description:

Geometric mean titers against each serotype with the dengue virus strain were assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil). Dengue subjects naïve at baseline are defined as those subjects with titers < 10 (1/dil) against all dengue serotypes at baseline.

End point type

Secondary

End point timeframe:

Post-Injection 3 and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 313 | 98 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Post-Injection 3 | 62.9 | 8.1 | | |
| CYD dengue Serotype 1; 1st year follow up | 20.9 | 5.6 | | |
| CYD dengue Serotype 1; 2nd year follow up | 16.1 | 5.9 | | |
| CYD dengue Serotype 1; 3rd year follow up | 12 | 2.9 | | |
| CYD dengue Serotype 1; 4th year follow up | 7.7 | 3.1 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 81.9 | 8.1 | | |
| CYD dengue Serotype 2; 1st year follow up | 38.6 | 2.8 | | |
| CYD dengue Serotype 2; 2nd year follow up | 49.1 | 5.9 | | |
| CYD dengue Serotype 2; 3rd year follow up | 30.6 | 2.9 | | |
| CYD dengue Serotype 2; 4th year follow up | 31.4 | 3.1 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 87 | 16.2 | | |
| CYD dengue Serotype 3; 1st year follow up | 59.5 | 2.9 | | |
| CYD dengue Serotype 3; 2nd year follow up | 53.6 | 5.9 | | |
| CYD dengue Serotype 3; 3rd year follow up | 45.8 | 2.9 | | |
| CYD dengue Serotype 3; 4th year follow up | 44.2 | 3.1 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 89.7 | 5.4 | | |
| CYD dengue Serotype 4; 1st year follow up | 69.6 | 0 | | |
| CYD dengue Serotype 4; 2nd year follow up | 67 | 8.8 | | |
| CYD dengue Serotype 4; 3rd year follow up | 62.6 | 2.9 | | |
| CYD dengue Serotype 4; 4th year follow up | 55.8 | 6.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 18 to 45 Years Immune at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|---|
| End point title | Percentage of Subjects Aged 18 to 45 Years Immune at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|---|

End point description:

Geometric mean titers against each serotype with the dengue virus strain were assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil). Dengue subjects immune at baseline are defined as those subjects with titers ≥ 10 (1/dil) against at least one dengue serotype at baseline.

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

End point timeframe:

Post-Injection 3 and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 114 | 47 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Post-Injection 3 | 89.3 | 70 | | |
| CYD dengue Serotype 1; 1st year follow up | 77.8 | 57.1 | | |
| CYD dengue Serotype 1; 2nd year follow up | 86.3 | 65 | | |
| CYD dengue Serotype 1; 3rd year follow up | 80.8 | 63.2 | | |
| CYD dengue Serotype 1; 4th year follow up | 84.8 | 66.7 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 91.1 | 65 | | |
| CYD dengue Serotype 2; 1st year follow up | 88.9 | 71.4 | | |
| CYD dengue Serotype 2; 2nd year follow up | 92.2 | 70 | | |
| CYD dengue Serotype 2; 3rd year follow up | 88.5 | 68.4 | | |
| CYD dengue Serotype 2; 4th year follow up | 91.5 | 66.7 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 98.2 | 60 | | |

| | | | | |
|---|------|------|--|--|
| CYD dengue Serotype 3; 1st year follow up | 90.7 | 66.7 | | |
| CYD dengue Serotype 3; 2nd year follow up | 98 | 70 | | |
| CYD dengue Serotype 3; 3rd year follow up | 94.2 | 73.7 | | |
| CYD dengue Serotype 3; 4th year follow up | 91.5 | 61.1 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 100 | 65 | | |
| CYD dengue Serotype 4; 1st year follow up | 98.1 | 47.6 | | |
| CYD dengue Serotype 4; 2nd year follow up | 96.1 | 45 | | |
| CYD dengue Serotype 4; 3rd year follow up | 100 | 42.1 | | |
| CYD dengue Serotype 4; 4th year follow up | 97.9 | 44.4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Aged 18 to 45 Years Naïve at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Percentage of Subjects Aged 18 to 45 Years Naïve at Baseline Who Are Seropositive for Each of the Dengue Virus Serotypes Up to 4 Years After The Third Vaccination With CYD Dengue Vaccine |
|-----------------|--|

End point description:

Geometric mean titers against each serotype with the dengue virus strain were assessed using a dengue plaque reduction neutralization test (PRNT) assay. Seropositive was defined as subjects with antibody titers ≥ 10 (1/dil). Dengue subjects naïve at baseline are defined as those subjects with titers < 10 (1/dil) against all dengue serotypes at baseline.

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

End point timeframe:

Post-Injection 3 and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 313 | 98 | | |
| Units: Percentage of subjects | | | | |
| number (not applicable) | | | | |
| CYD dengue Serotype 1; Post-Injection 3 | 59.4 | 14.3 | | |
| CYD dengue Serotype 1; 1st year follow up | 21.3 | 9.5 | | |
| CYD dengue Serotype 1; 2nd year follow up | 10.2 | 5.3 | | |
| CYD dengue Serotype 1; 3rd year follow up | 7.1 | 0 | | |

| | | | | |
|---|------|------|--|--|
| CYD dengue Serotype 1; 4th year follow up | 5.6 | 0 | | |
| CYD dengue Serotype 2; Post-Injection 3 | 73.4 | 0 | | |
| CYD dengue Serotype 2; 1st year follow up | 49.2 | 14.3 | | |
| CYD dengue Serotype 2; 2nd year follow up | 50.8 | 0 | | |
| CYD dengue Serotype 2; 3rd year follow up | 28.6 | 5.6 | | |
| CYD dengue Serotype 2; 4th year follow up | 26.4 | 0 | | |
| CYD dengue Serotype 3; Post-Injection 3 | 87.5 | 14.3 | | |
| CYD dengue Serotype 3; 1st year follow up | 48.3 | 14.3 | | |
| CYD dengue Serotype 3; 2nd year follow up | 61 | 21.1 | | |
| CYD dengue Serotype 3; 3rd year follow up | 46.3 | 0 | | |
| CYD dengue Serotype 3; 4th year follow up | 28.3 | 0 | | |
| CYD dengue Serotype 4; Post-Injection 3 | 87.5 | 4.8 | | |
| CYD dengue Serotype 4; 1st year follow up | 78.7 | 14.3 | | |
| CYD dengue Serotype 4; 2nd year follow up | 71.2 | 5.3 | | |
| CYD dengue Serotype 4; 3rd year follow up | 66.1 | 0 | | |
| CYD dengue Serotype 4; 4th year follow up | 63 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Antibodies In Subjects 18 to 45 Years Old Against Each Serotype with the Parental Dengue Virus Strain Before and Following The Third Injection with CYD Dengue Vaccine

| | |
|-----------------|--|
| End point title | Geometric Mean Titers (GMTs) of Antibodies In Subjects 18 to 45 Years Old Against Each Serotype with the Parental Dengue Virus Strain Before and Following The Third Injection with CYD Dengue Vaccine |
|-----------------|--|

End point description:

Geometric mean titers against each serotype with the dengue virus strain were assessed using a dengue plaque reduction neutralization test (PRNT) assay.

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

End point timeframe:

Pre-Injection 1, Post-Injection 3, and up to 4 years of follow up

| End point values | CYD Dengue vaccine group | Control group | | |
|---|--------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 438 | 147 | | |
| Units: Titers (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| CYD dengue Serotype 1; Pre-Injection 1 | 15.8 (11.7 to 21.5) | 19.2 (10.9 to 33.9) | | |
| CYD dengue Serotype 1; Post-Injection 3 | 48.7 (33.6 to 70.4) | 16.2 (9.77 to 27) | | |
| CYD dengue Serotype 1; 1st year follow up | 26.3 (17.9 to 38.6) | 15.2 (8.76 to 26.3) | | |
| CYD dengue Serotype 1; 2nd year follow up | 26.3 (17.7 to 38.9) | 16.3 (9.09 to 29.3) | | |
| CYD dengue Serotype 1; 3rd year follow up | 24.1 (15.9 to 36.5) | 13.9 (7.89 to 24.6) | | |
| CYD dengue Serotype 1; 4th year follow up | 23.5 (15.5 to 35.5) | 14.4 (8.03 to 25.6) | | |
| CYD dengue Serotype 2; Pre-Injection 1 | 16.9 (12.3 to 23.1) | 21 (11.5 to 38.2) | | |
| CYD dengue Serotype 2; Post-Injection 3 | 66.9 (47.9 to 93.5) | 15.2 (8.61 to 27) | | |
| CYD dengue Serotype 2; 1st year follow up | 50.4 (34.5 to 73.7) | 19.3 (10.7 to 34.7) | | |
| CYD dengue Serotype 2; 2nd year follow up | 66.5 (43.7 to 101) | 20 (10.2 to 39) | | |
| CYD dengue Serotype 2; 3rd year follow up | 38.4 (25.8 to 57.2) | 17 (9.38 to 30.8) | | |
| CYD dengue Serotype 2; 4th year follow up | 32.9 (22.4 to 48.2) | 15.5 (8.51 to 28.2) | | |
| CYD dengue Serotype 3; Pre-Injection 1 | 14.5 (11.2 to 18.7) | 19.4 (11.4 to 33.1) | | |
| CYD dengue Serotype 3; Post-Injection 3 | 88.4 (68.6 to 114) | 13.3 (8.22 to 21.7) | | |
| CYD dengue Serotype 3; 1st year follow up | 45.2 (32.1 to 63.6) | 14.8 (8.96 to 24.3) | | |
| CYD dengue Serotype 3; 2nd year follow up | 64.8 (46.8 to 89.7) | 19.9 (11.5 to 34.5) | | |
| CYD dengue Serotype 3; 3rd year follow up | 48.3 (33 to 70.8) | 14.7 (8.46 to 25.7) | | |
| CYD dengue Serotype 3; 4th year follow up | 28.6 (20.2 to 40.6) | 11.8 (7.18 to 19.3) | | |
| CYD dengue Serotype 4; Pre-Injection 1 | 10.1 (8.03 to 12.7) | 11.7 (7.74 to 17.6) | | |
| CYD dengue Serotype 4; Post-Injection 3 | 122 (96.5 to 155) | 10 (6.96 to 14.4) | | |
| CYD dengue Serotype 4; 1st year follow up | 70.3 (53.6 to 92.2) | 9.87 (6.88 to 14.2) | | |
| CYD dengue Serotype 4; 2nd year follow up | 52.6 (39.9 to 69.3) | 8.5 (6.07 to 11.9) | | |
| CYD dengue Serotype 4; 3rd year follow up | 46.4 (35.5 to 60.6) | 8.39 (5.83 to 12.1) | | |
| CYD dengue Serotype 4; 4th year follow up | 32.6 (25.2 to 42.3) | 7.54 (5.69 to 10) | | |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from Day 0 (post-vaccination) up to the 4th year of follow up.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 11.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | CYD Dengue vaccine group |
|-----------------------|--------------------------|

Reporting group description:

Subjects received the CYD dengue vaccine at 0, 6, and 12 months as first, second, and third vaccinations, respectively.

| | |
|-----------------------|---------------|
| Reporting group title | Control group |
|-----------------------|---------------|

Reporting group description:

Subjects received a placebo at first vaccination (Month 0). Subjects <12 years received hepatitis A at second (Month 6) and third (Month 12) vaccinations. Subjects ≥12 years received influenza vaccine of Northern and Southern hemisphere formulations at second (Month 6) and third (Month 12) vaccinations.

| Serious adverse events | CYD Dengue vaccine group | Control group | |
|---|--------------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 43 / 898 (4.79%) | 13 / 300 (4.33%) | |
| number of deaths (all causes) | 3 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute leukaemia | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute lymphocytic leukaemia | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Ovarian cancer metastatic | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Ovarian germ cell teratoma benign | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 898 (0.00%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 0 / 898 (0.00%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Osteotomy | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ruptured ectopic pregnancy | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 898 (0.00%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 2 / 898 (0.22%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 898 (0.00%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand fracture | | | |
| subjects affected / exposed | 0 / 898 (0.00%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intentional overdose | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic haematoma | | | |
| subjects affected / exposed | 0 / 898 (0.00%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Nervous system disorders | | | |
| Migraine | | | |
| subjects affected / exposed | 2 / 898 (0.22%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radial nerve palsy | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope vasovagal | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tension headache | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Colitis | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid disorder | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 0 / 898 (0.00%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 898 (0.00%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (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 | | | |
| Appendicitis | | | |
| subjects affected / exposed | 2 / 898 (0.22%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Conjunctivitis viral | | | |
| subjects affected / exposed | 2 / 898 (0.22%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Corneal infection | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dengue fever | | | |
| subjects affected / exposed | 3 / 898 (0.33%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 898 (0.22%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 2 / 300 (0.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Groin abscess | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 2 / 898 (0.22%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpangina | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymph node tuberculosis | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis viral | | | |
| subjects affected / exposed | 0 / 898 (0.00%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis bacterial | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 1 / 300 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 898 (0.22%) | 0 / 300 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 898 (0.11%) | 0 / 300 (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 | CYD Dengue vaccine group | Control group | |
|---|--------------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 481 / 898 (53.56%) | 198 / 300 (66.00%) | |
| Nervous system disorders | | | |
| Headache; Post-Any Injection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[1] | 402 / 891 (45.12%) | 114 / 297 (38.38%) | |
| occurrences (all) | 402 | 114 | |
| General disorders and administration site conditions | | | |
| Injection site Pain; Post-Any Injection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[2] | 481 / 892 (53.92%) | 198 / 297 (66.67%) | |
| occurrences (all) | 481 | 198 | |
| Injection site Erythema; Post-Any Injection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[3] | 64 / 891 (7.18%) | 45 / 297 (15.15%) | |
| occurrences (all) | 64 | 45 | |
| Injection site Swelling; Post-Any Injection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[4] | 37 / 892 (4.15%) | 25 / 297 (8.42%) | |
| occurrences (all) | 37 | 25 | |
| Fever; Post-Any Injection | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---------------------------|---------------------------|--|
| subjects affected / exposed ^[5] occurrences (all) | 101 / 892 (11.32%) 101 | 22 / 297 (7.41%) 22 | |
| Malaise; Post-Any Injection alternative assessment type: Systematic subjects affected / exposed ^[6] occurrences (all) | 372 / 891 (41.75%) 372 | 105 / 297 (35.35%) 105 | |
| Asthenia; Post-Any Injection alternative assessment type: Systematic subjects affected / exposed ^[7] occurrences (all) | 183 / 891 (20.54%) 183 | 52 / 297 (17.51%) 52 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 42 / 898 (4.68%) 48 | 15 / 300 (5.00%) 17 | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 42 / 898 (4.68%) 47 | 15 / 300 (5.00%) 15 | |
| Musculoskeletal and connective tissue disorders Myalgia; Post-Any Injection alternative assessment type: Systematic subjects affected / exposed ^[8] occurrences (all) | 394 / 891 (44.22%) 394 | 130 / 297 (43.77%) 130 | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 72 / 898 (8.02%) 77 | 27 / 300 (9.00%) 30 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited event recorded in a diary within 14 days after any injection; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited event recorded in a diary within 7 days after any injection; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited event recorded in a diary within 7 days after any injection; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited event recorded in a diary within 7 days after any injection; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited event recorded in a diary within 14 days after any injection; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited event recorded in a diary within 14 days after any injection; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited event recorded in a diary within 14 days after any injection; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was a solicited event recorded in a diary within 14 days after any injection; the total number (N) reflects those subjects for which the diary cards were returned and for which data were available for the event during the period.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 05 December 2008 | Integrated comments from the Institutional Review Boards in the Protocol and Appendices. |
| 20 May 2009 | Modified the observer-blind design for the second vaccination into a single-blind design and modified the interim statistical analysis schedule to include an analysis at 24 and 36 months post-last vaccination to get supportive data regarding persistence of neutralizing antibodies. |
| 06 December 2010 | Changed from Pan Flavivirus reverse transcriptase-polymerase chain reaction (RT-PCR) to dengue screen RT-PCR to improve assay sensitivity, replaced the microneutralization assay by the plaque reduction neutralization test (PRNT) assay to determine dengue neutralizing antibodies to serotypes 1, 2, 3, and 4 in subjects, replaced the method of the assessment of the cross-reactivity (microneutralization assay) by a seroneutralization assay, added an observational objective regarding the cell mediated immunity and additional blood sample volumes were added at each visit during the 4-year follow up, and due to limited time between post-Injection 2 and 3 results the post-Injection 2 analysis of safety and immunogenicity was cancelled in order to analyze the results of post-Injection 2 and 3 samples obtained by PRNT at the same time; as a result, the blind was broken and subjects were informed about the vaccines after the database lock for statistical analyses. |
| 28 March 2012 | The Sponsor's Responsible Medical Officer for the study was replaced by T. Anh Wartel during the conduct of the long-term follow up and a new Principal Investigator (Low Chian Yong) was assigned to Center 004 from July 2011 following the resignation of the existing Principal Investigator. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported