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)	EMEA-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

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

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 administrated 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		

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]

End point description:

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

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

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

No statistical analyses for this end point

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

No statistical analyses for this end point

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

No statistical analyses for this end point

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

	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	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

No statistical analyses for this end point

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