Clinical trial results:
Long-Term Safety Follow-Up of Thai Children Who Were Included in an Efficacy Study of a Tetravalent Dengue Vaccine

Summary

EudraCT number	2014-001737-88
Trial protocol	Outside EU/EEA
Global end of trial date	19 February 2016

Results information

Result version number	v2 (current)
This version publication date	23 August 2018
First version publication date	19 May 2016
Version creation reason	• New data added to full data set Follow-up data up to Year 4 were added to the full data set

Trial information

Trial identification

Sponsor protocol code	CYD57

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01983553
WHO universal trial number (UTN)	U1111-1127-7380

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	14 Espace Henry Vallée, Lyon, France, 69007
Public contact	Trial Transparency, Sanofi Pasteur, RegistryContactUs@sanofipasteur.com
Scientific contact	Trial Transparency, Sanofi Pasteur, RegistryContactUs@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	20 October 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to evaluate the continuous long-term follow-up of hospitalized dengue and safety of subjects who received CYD dengue vaccine in study CYD23 (EudraCT No. 2014-001710-25) including retrospective data collection (i.e., including the blood samples collected from March 05th, 2012 to September 9th, 2013) and prospective data collection from CYD57 study start (September 10th, 2013) until the end of the study, and the following activities will be performed.
1) To describe the incidence of virologically-confirmed hospitalized dengue cases.
2) To characterize hospitalized dengue cases.
3) To evaluate the occurrence of related and fatal serious adverse events (SAEs).

Protection of trial subjects:

Subjects were vaccinated in a previous study, CYD23. No vaccination was administered as part of this study.

Background therapy:

In study CYD23, subjects age 4 to 11 were randomized to receive 3 injections of either CYD dengue vaccine or control, 1 each at 0, 6, and 12 months. Those that received at least one injection were eligible to be included in this follow-up study.

Evidence for comparator:

Not applicable

Actual start date of recruitment	10 September 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Thailand: 3203
Worldwide total number of subjects	3203
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)	3203
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects were enrolled in the original study CYD23 from 10 September 2013 to 29 November 2013 at 1 clinic center in Thailand.

Pre-assignment

Screening details:

Of the 3997 subjects who were treated in the original study CYD23, a total of 3203 subjects were included in the 4-year safety follow-up CYD57 study.

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:

Subjects and site staff remained blinded to the treatment allocation in CYD23 until the end of the study (CYD57) to avoid any bias in the safety follow-up (detection of dengue cases). In the event of an emergency (i.e., serious adverse event), the code of CYD57 could be broken by the Investigator as explained in the code-breaking procedures described in the Operating Guidelines.

Arms

Are arms mutually exclusive?	Yes
Arm title	CYD Dengue Vaccine Group

Arm description:

Subjects received 3 injections of CYD dengue vaccine, 1 injection each at 0, 6, and 12 months in study CYD23.

Arm type	Experimental
Investigational medicinal product name	CYD Dengue vaccine
Investigational medicinal product code	
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 in the initial CYD23 study.

Arm title	Control Group

Arm description:

Subjects received either Rabies vaccine (Verorab®) or placebo control as a first injection on Day 0, placebo for second and third injections at 6 and 12 months, respectively, in the original CYD23 study.

Arm type	Active comparator
Investigational medicinal product name	Placebo (sodium chloride)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL, subcutaneous, 1 injection of either Verorab or placebo as a first injection on Day 0, placebo for second and third injections at 6 and 12 months, respectively, in the original CYD23 study.

Investigational medicinal product name	Rabies vaccine (Verorab®)
Investigational medicinal product code	
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 of either Verorab or placebo as a first injection on Day 0, placebo for second and third injections at 6 and 12 months, respectively, in the original CYD23 study.

Number of subjects in period 1	CYD Dengue Vaccine Group	Control Group
Started	2131	1072
Completed	2131	1072

Baseline characteristics

Reporting groups	
Reporting group title	CYD Dengue Vaccine Group
Reporting group description:	
Subjects received 3 injections of CYD dengue vaccine, 1 injection each at 0, 6, and 12 months in study CYD23.	
Reporting group title	Control Group
Reporting group description:	
Subjects received either Rabies vaccine (Verorab®) or placebo control as a first injection on Day 0, placebo for second and third injections at 6 and 12 months, respectively, in the original CYD23 study.	

Reporting group values	CYD Dengue Vaccine Group	Control Group	Total
Number of subjects	2131	1072	3203
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)	2131	1072	3203
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	8.11	8.15	
standard deviation	± 2.02	± 2.06	-
Gender categorical Units: Subjects			
Female	1118	579	1697
Male	1013	493	1506

End points

End points reporting groups

Reporting group title	CYD Dengue Vaccine Group

Reporting group description:

Subjects received 3 injections of CYD dengue vaccine, 1 injection each at 0, 6, and 12 months in study CYD23.

Reporting group title	Control Group

Reporting group description:

Subjects received either Rabies vaccine (Verorab®) or placebo control as a first injection on Day 0, placebo for second and third injections at 6 and 12 months, respectively, in the original CYD23 study.

Primary: Annual Incidence of Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study

End point title	Annual Incidence of Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study

End point description:

Annual incidence rate was defined as the cases among the number of subjects present at the beginning of each period (M) multiplied by 100 converted in annual rate (Annual incidence rate = Cases among M*100). Analysis was performed on Follow-up Analysis Set (FupAS) which included all subjects who were included in study CYD57.

End point type	Primary

End point timeframe:

Year 1 to Year 4 post-vaccination

End point values	CYD Dengue Vaccine Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2131	1072		
Units: Annual incidence rate				
number (confidence interval 95%)				
Any of the 4 Serotypes	1.0 (0.8 to 1.2)	1.1 (0.8 to 1.4)		
Serotype 1	0.2 (0.2 to 0.4)	0.3 (0.1 to 0.5)		
Serotype 2	0.3 (0.2 to 0.5)	0.3 (0.1 to 0.5)		
Serotype 3	0.2 (0.2 to 0.4)	0.2 (0.1 to 0.4)		
Serotype 4	0.2 (0.1 to 0.3)	0.3 (0.1 to 0.5)		
Unserotyped	0.0 (0.0 to 0.0)	0.1 (0.0 to 0.2)		

Statistical analyses

Statistical analysis title	Relative risk; Any of the 4 Serotypes

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Any of the 4 Serotypes

between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Relative Risk
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.36

Notes:

[1] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative risk; Serotype 1

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 1 between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	Relative Risk
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	2.21

Notes:

[2] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative risk; Serotype 2

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 2 between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Relative Risk
Point estimate	1.326
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	2.94

Notes:

[3] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative risk; Serotype 3

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 3 between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[4]
Parameter estimate	Relative Risk
Point estimate	1.056
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	2.51

Notes:

[4] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative risk; Serotype 4

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 4 between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[5]
Parameter estimate	Relative Risk
Point estimate	0.629
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	1.47

Notes:

[5] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative risk; Unserotyped

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Unserotyped between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Relative Risk
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1.22

Notes:

[6] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Primary: Number of Cases and Episodes of Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study

End point title	Number of Cases and Episodes of Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study[7]

End point description:

Cases were defined as the number of subjects with at least one hospitalized virologically-confirmed dengue episode. Episodes were defined as the number of hospitalized virologically-confirmed dengue episodes. Analysis was performed on FupAS.

End point type	Primary

End point timeframe:

Year 1 to Year 4 post-vaccination

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	2131	1072		
Units: Number of cases and episodes of dengue				
number (not applicable)				
Cases; Any of the 4 Serotypes	85	46		
Episodes; Any of the 4 Serotypes	85	46		
Cases; Serotype 1	21	11		
Episodes; Serotype 1	21	11		
Cases; Serotype 2	29	11		
Episodes; Serotype 2	29	11		
Cases; Serotype 3	21	10		
Episodes; Serotype 3	21	10		
Cases; Serotype 4	15	12		
Episodes; Serotype 4	15	12		
Cases; Unserotyped	0	3		
Episodes; Unserotyped	0	3		

Statistical analyses

No statistical analyses for this end point

Primary: Annual Incidence of Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Collected By Age Group Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study

End point title	Annual Incidence of Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Collected By Age Group Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study

End point description:

Annual incidence rate was defined as the cases among the number of subjects present at the beginning of each period (M) multiplied by 100 converted in annual rate (Annual incidence rate = Cases among M*100). Analysis was performed on FupAS. Here, "n" signifies number of subjects evaluable for each specified category. Endpoint values <0.1 were rounded to 0.1.

End point type	Primary

End point timeframe:

Year 1 to Year 4 post-vaccination

End point values	CYD Dengue Vaccine Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2131	1072		
Units: Incidence rate				
number (confidence interval 95%)				
4 to 5 Years: Any of the 4 Serotypes (n=393, 192)	1.7 (1.1 to 2.4)	1.2 (0.5 to 2.2)		
6 to 11 Years: Any of the 4 Serotypes(n=1738, 880)	0.8 (0.6 to 1.1)	1.1 (0.7 to 1.4)		
4 to 5 Years: Serotype 1 (n=393, 192)	0.6 (0.3 to 1.2)	0.1 (0.0 to 0.7)		
6 to 11 Years: Serotype 1 (n=1738, 880)	0.2 (0.1 to 0.3)	0.3 (0.1 to 0.5)		
4 to 5 Years: Serotype 2 (n=393, 192)	0.4 (0.1 to 0.8)	0.1 (0.0 to 0.7)		
6 to 11 Years: Serotype 2 (n=1738, 880)	0.3 (0.2 to 0.5)	0.3 (0.1 to 0.5)		
4 to 5 Years: Serotype 3 (n=393, 192)	0.3 (0.1 to 0.7)	0.3 (0.0 to 0.9)		
6 to 11 Years: Serotype 3 (n=1738, 880)	0.2 (0.1 to 0.4)	0.2 (0.1 to 0.4)		
4 to 5 Years: Serotype 4 (n=393, 192)	0.4 (0.1 to 0.8)	0.4 (0.1 to 1.1)		
6 to 11 Years: Serotype 4 (n=1738, 880)	0.1 (0.1 to 0.2)	0.3 (0.1 to 0.5)		
4 to 5 Years: Unserotyped (n=393, 192)	0.0 (0.0 to 0.2)	0.3 (0.0 to 0.9)		
6 to 11 Years: Unserotyped (n=1738, 880)	0.0 (0.0 to 0.1)	0.1 (0.0 to 0.2)		

Statistical analyses

Statistical analysis title	Relative Risk; 4 to 5 years; Any Serotype

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Any of the 4 Serotypes (4 to 5 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 525 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group

Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[8]
Parameter estimate	Relative Risk
Point estimate	1.411
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	3.42

Notes:

[8] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 6 to 11 years; Any Serotype

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Any of the 4 Serotypes (6 to 11 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 2618 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	Relative Risk
Point estimate	0.807
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.25

Notes:

[9] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 4 to 5 years; Serotype 1

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 1 (4 to 5 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 525 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	Relative Risk
Point estimate	4.885
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	212.02

Notes:

[10] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 6 to 11 years; Serotype 1

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 1 (6 to 11 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 2618 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Relative Risk
Point estimate	0.557
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	1.46

Notes:

[11] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 4 to 5 years; Serotype 2

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 2 (4 to 5 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 525 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[12]
Parameter estimate	Relative Risk
Point estimate	2.931
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	134.83

Notes:

[12] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 6 to 11 years; Serotype 2

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 2 (6 to 11 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 2618 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[13]
Parameter estimate	Relative Risk
Point estimate	1.165

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	2.74

Notes:

[13] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 4 to 5 years; Serotype 3

Statistical analysis description:

Relative risk analysis of the annual incidence rate at Year 1 for Serotype 3 (4 to 5 year) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 525 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[14]
Parameter estimate	Relative Risk
Point estimate	1.221
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	12.83

Notes:

[14] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 6 to 11 years; Serotype 3

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 3 (6 to 11 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 2618 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[15]
Parameter estimate	Relative Risk
Point estimate	1.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	2.73

Notes:

[15] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 4 to 5 years; Serotype 4

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 4 (4 to 5 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 525 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[16]
Parameter estimate	Relative Risk
Point estimate	0.977
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	6.04

Notes:

[16] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 6 to 11 years; Serotype 4

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 4 (6 to 11 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 2618 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[17]
Parameter estimate	Relative Risk
Point estimate	0.506
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	1.44

Notes:

[17] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 4 to 5 years; Unserotyped

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Unserotyped (4 to 5 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 525 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[18]
Parameter estimate	Relative Risk
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2.6

Notes:

[18] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; 6 to 11 years; Unserotyped

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Unserotyped (6 to 11 years) between the CYD Dengue vaccine group and the Control group. Total number of subjects analysed were 2618 instead of 3203.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[19]
Parameter estimate	Relative Risk
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	19.75

Notes:

[19] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Primary: Number of Cases and Episodes of Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Collected By Age Group Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study

End point title	Number of Cases and Episodes of Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Collected By Age Group Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study[20]

End point description:

Cases were defined as the number of subjects with at least one hospitalized virologically-confirmed dengue episode. Episodes were defined as the number of hospitalized virologically-confirmed dengue episodes. Analysis was performed on FupAS. Here, "n" signifies number of subjects evaluable for each specified category.

End point type	Primary

End point timeframe:

Year 1 to Year 4 post-vaccination

Notes:

[20] - 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	2131	1072		
Units: Number of cases and episodes of dengue				
number (not applicable)				
4to5 years cases:Any of the 4 Serotypes(n=393,192)	26	9		
4to5 years episodes: Any of 4 Serotypes(n=393,192)	26	9		

6to11years cases:Any of the 4Serotypes(n=1738,880)	59	37		
6to11years episodes:Any of 4 Serotypes(n=1738,880)	59	37		
4 to 5 years cases: Serotype 1 (n=393, 192)	10	1		
4 to 5 years episodes: Serotype 1 (n=393, 192)	10	1		
6 to 11 years cases: Serotype 1 (n=1738,880)	11	10		
6 to 11 years episodes: Serotype 1 (n=1738,880)	11	10		
4 to 5 years cases: Serotype 2 (n=393, 192)	6	1		
4 to 5 years episodes: Serotype 2 (n=393, 192)	6	1		
6 to 11 years cases: Serotype 2 (n=1738,880)	23	10		
6 to 11 years episodes: Serotype 2 (n=1738,880)	23	10		
4 to 5 years cases: Serotype 3 (n=393, 192)	5	2		
4 to 5 years episodes: Serotype 3 (n=393, 192)	5	2		
6 to 11 years cases: Serotype 3 (n=1738,880)	16	8		
6 to 11 years episodes: Serotype 3 (n=1738,880)	16	8		
4 to 5 years cases: Serotype 4 (n=393, 192)	6	3		
4 to 5 years episodes: Serotype 4 (n=393, 192)	6	3		
6 to 11 years cases: Serotype 4 (n=1738,880)	9	9		
6 to 11 years episodes: Serotype 4 (n=1738,880)	9	9		
4 to 5 years cases: Unserotyped (n=393, 192)	0	2		
4 to 5 years episodes: Unserotyped (n=393, 192)	0	2		
6 to 11 years cases: Unserotyped (n=1738,880)	0	1		
6 to 11 years episodes: Unserotyped (n=1738,880)	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Annual Incidence of Clinically Severe Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study

End point title	Annual Incidence of Clinically Severe Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Following Vaccination with Either CYD Dengue Vaccine or a Placebo in a Previous Study[21]

End point description:

Annual incidence rate was defined as the cases among the number of subjects present at the beginning

of each period (M) multiplied by 100 converted in annual rate (Annual incidence rate = Cases among M*100). Analysis was performed on FupAS. Endpoint values <0.1 were rounded to 0.1.

End point type	Primary

End point timeframe:

Year 1 to Year 4 post-vaccination

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: 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	2131	1072		
Units: Annual incidence rate				
number (confidence interval 95%)				
Any of the 4 Serotypes	0.1 (0.0 to 0.2)	0.1 (0.0 to 0.2)		
Serotype 1	0.1 (0.0 to 0.2)	0.0 (0.0 to 0.1)		
Serotype 2	0.1 (0.0 to 0.1)	0.1 (0.0 to 0.1)		
Serotype 3	0.1 (0.0 to 0.1)	0.0 (0.0 to 0.1)		
Serotype 4	0.1 (0.0 to 0.1)	0.1 (0.0 to 0.2)		
Unserotyped	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Cases and Episodes of Clinically Severe Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Following Vaccination with CYD Dengue Vaccine or Placebo in a Previous Study

End point title	Number of Cases and Episodes of Clinically Severe Hospitalized Virologically-Confirmed Dengue Due to Any and Each Serotype Following Vaccination with CYD Dengue Vaccine or Placebo in a Previous Study[22]

End point description:

Cases were defined as the number of subjects with at least one hospitalized virologically-confirmed dengue episode. Episodes were defined as the number of hospitalized virologically-confirmed dengue episodes. Analysis was performed on FupAS.

End point type	Primary

End point timeframe:

Year 1 to Year 4 post-vaccination

Notes:

[22] - 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	2131	1072		
Units: Number of cases and episodes				
number (not applicable)				
Cases: Any of the 4 Serotypes	8	3		
Episodes: Any of the 4 Serotypes	8	3		
Cases: Serotype 1	6	0		
Episodes: Serotype 1	6	0		
Cases: Serotype 2	1	1		
Episodes: Serotype 2	1	1		
Cases: Serotype 3	1	0		
Episodes: Serotype 3	1	0		
Cases: Serotype 4	1	2		
Episodes: Serotype 4	1	2		
Cases: Unserotyped	0	0		
Episodes: Unserotyped	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Non-Serotype Specific Dengue Viremia Among Hospitalized Virologically-Confirmed Dengue Cases Following Vaccination with CYD Dengue Vaccine or Placebo in a Previous Study

End point title	Number of Subjects with Non-Serotype Specific Dengue Viremia Among Hospitalized Virologically-Confirmed Dengue Cases Following Vaccination with CYD Dengue Vaccine or Placebo in a Previous Study[23]

End point description:

Quantified viremia was defined as >= lower limit of quantitation (log10 plaque forming unit [pfu]/mL). Analysis was performed on FupAS.

End point type	Primary

End point timeframe:

Year 1 to Year 4 post-vaccination at each of the following time points: Anytime, 0-3 days, 4-7 days, 0-7 days, After 7 days.

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: 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	2131	1072		
Units: Number of subjects				
number (not applicable)				
Cases - Anytime	78	42		
Mean Viremia - Anytime	3.64	3.38		
Cases - 0-3 days	25	12		
Mean Viremia - 0-3 days	4.35	3.83		

Cases - 4-7 days	53	27		
Mean Viremia - 4-7 days	3.31	3.12		
Cases - 0-7 days	78	39		
Mean Viremia - 0-7 days	3.64	3.34		
Cases - After 7 days	0	3		
Mean Viremia - After 7 days	0	3.88		

Statistical analyses

No statistical analyses for this end point

Primary: Annual Incidence of Hospitalized Virologically-Confirmed Dengue Cases Due to Any and Each Serotype and Meeting WHO 1997 Criteria Collected During Entire Passive Surveillance After Previous Vaccination with Either CYD Dengue Vaccine or Placebo

End point title	Annual Incidence of Hospitalized Virologically-Confirmed Dengue Cases Due to Any and Each Serotype and Meeting WHO 1997 Criteria Collected During Entire Passive Surveillance After Previous Vaccination with Either CYD Dengue Vaccine or Placebo

End point description:

Annual incidence rate was defined as the cases among the number of subjects present at the beginning of each period (M) multiplied by 100 converted in annual rate (Annual incidence rate = Cases among M*100). Analysis was performed on FupAS. Endpoint values <0.1 were rounded to 0.1.

End point type	Primary

End point timeframe:

Year 1 to Year 4 post-vaccination

End point values	CYD Dengue Vaccine Group	Control Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2131	1072		
Units: Annual incidence rate				
number (confidence interval 95%)				
Any of the 4 Serotypes Any grade	0.1 (0.0 to 0.2)	0.1 (0.0 to 0.2)		
Any of the 4 Serotypes Grade I	0.1 (0.0 to 0.1)	0.1 (0.0 to 0.2)		
Any of the 4 Serotypes Grade II	0.1 (0.0 to 0.1)	0.1 (0.0 to 0.1)		
Any of the 4 Serotypes Grade III	0.1 (0.0 to 0.1)	0.0 (0.0 to 0.1)		
Any of the 4 Serotypes Grade IV	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Serotype 1 Any grade	0.1 (0.0 to 0.1)	0.0 (0.0 to 0.1)		
Serotype 1 Grade I	0.1 (0.0 to 0.1)	0.0 (0.0 to 0.1)		
Serotype 1 Grade II	0.1 (0.0 to 0.1)	0.0 (0.0 to 0.1)		
Serotype 1 Grade III	0.1 (0.0 to 0.1)	0.0 (0.0 to 0.1)		
Serotype 1 Grade IV	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Serotype 2 Any grade	0.1 (0.0 to 0.1)	0.1 (0.0 to 0.1)		
Serotype 2 Grade I	0.1 (0.0 to 0.1)	0.1 (0.0 to 0.1)		
Serotype 2 Grade II	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Serotype 2 Grade III	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Serotype 2 Grade IV	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		

Serotype 3 Any grade	0.1 (0.0 to 0.1)	0.0 (0.0 to 0.1)		
Serotype 3 Grade I	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Serotype 3 Grade II	0.1 (0.0 to 0.1)	0.0 (0.0 to 0.1)		
Serotype 3 Grade III	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Serotype 3 Grade IV	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Serotype 4 Any grade	0.1 (0.0 to 0.1)	0.1 (0.0 to 0.2)		
Serotype 4 Grade I	0.0 (0.0 to 0.0)	0.1 (0.0 to 0.1)		
Serotype 4 Grade II	0.1 (0.0 to 0.1)	0.1 (0.0 to 0.1)		
Serotype 4 Grade III	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Serotype 4 Grade IV	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Unserotyped Any grade	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Unserotyped Grade I	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Unserotyped Grade II	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Unserotyped Grade III	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		
Unserotyped Grade IV	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.1)		

Statistical analyses

Statistical analysis title	Relative Risk; Any serotype; Any grade

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Any of the 4 Serotypes Any grade between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[24]
Parameter estimate	Relative Risk
Point estimate	1.174
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	7.03

Notes:

[24] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; Any serotype; Grade I

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Any of the 4 Serotypes Grade I between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[25]
Parameter estimate	Relative Risk
Point estimate	0.252

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	4.83

Notes:

[25] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; Any serotype; Grade II

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Any of the 4 Serotypes Grade II between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[26]
Parameter estimate	Relative Risk
Point estimate	2.012
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	99.1

Notes:

[26] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; Serotype 2; Any grade

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 2 Any grade between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[27]
Parameter estimate	Relative Risk
Point estimate	0.503
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	39.49

Notes:

[27] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; Serotype 2; Grade I

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 2 Grade I between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group

Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[28]
Parameter estimate	Relative Risk
Point estimate	0.503
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	39.49

Notes:

[28] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; Serotype 4; Any grade

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 4 Any grade between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[29]
Parameter estimate	Relative Risk
Point estimate	0.252
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	4.83

Notes:

[29] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; Serotype 4; Grade I

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 4 Grade I between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[30]
Parameter estimate	Relative Risk
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	19.62

Notes:

[30] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Statistical analysis title	Relative Risk; Serotype 4; Grade II

Statistical analysis description:

Relative risk analysis of the annual incidence rate during Year 1 to Year 4 for Serotype 4 Grade II between the CYD Dengue vaccine group and the Control group.

Comparison groups	CYD Dengue Vaccine Group v Control Group
Number of subjects included in analysis	3203
Analysis specification	Pre-specified
Analysis type	other[31]
Parameter estimate	Relative Risk
Point estimate	0.503
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	39.49

Notes:

[31] - The 95% confidence interval of the relative risk is calculated using the Exact method described by Breslow and Day.

Primary: Number of Cases and Episodes of Hospitalized Virologically-Confirmed Dengue Cases Due to Any and Each Serotype and Meeting WHO 1997 Criteria Following Vaccination with CYD Dengue Vaccine or Placebo in a Previous Study

End point title	Number of Cases and Episodes of Hospitalized Virologically-Confirmed Dengue Cases Due to Any and Each Serotype and Meeting WHO 1997 Criteria Following Vaccination with CYD Dengue Vaccine or Placebo in a Previous Study[32]

End point description:

Cases were defined as the number of subjects with at least one hospitalized virologically-confirmed dengue episode meeting WHO criteria. Episodes are defined as the number of hospitalized virologically-confirmed dengue episodes meeting WHO criteria. Grade I: Fever accompanied by non-specific constitutional symptoms; the only hemorrhagic manifestation is a positive tourniquet test. Grade II: Spontaneous bleeding in addition to the manifestations of Grade I subjects, usually in the form of skin and/or other hemorrhages. Grade III: Circulatory failure manifested by rapid and weak pulse, narrowing of pulse pressure (20 mmHg or less) or hypotension, with the presence of cold clammy skin and restlessness. Grade IV: Profound shock with undetectable blood pressure and pulse. Analysis was performed on FupAS.

End point type	Primary

End point timeframe:

Year 1 to Year 4 post-vaccination

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: 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	2131	1072		
Units: Number of cases and episodes				
number (not applicable)				
Cases: Any of the 4 Serotypes Any grade	7	3		
Episodes: Any of the 4 Serotypes Any grade	7	3		
Cases: Any of the 4 Serotypes Grade I	1	2		
Episodes: Any of the 4 Serotypes Grade I	1	2		
Cases: Any of the 4 Serotypes Grade II	4	1		

Episodes: Any of the 4 Serotypes Grade II	4	1		
Cases: Any of the 4 Serotypes Grade III	2	0		
Episodes: Any of the 4 Serotypes Grade III	2	0		
Cases: Any of the 4 Serotypes Grade IV	0	0		
Episodes: Any of the 4 Serotypes Grade IV	0	0		
Cases: Serotype 1 Any grade	5	0		
Episodes: Serotype 1 Any grade	5	0		
Cases: Serotype 1 Grade I	1	0		
Episodes: Serotype 1 Grade I	1	0		
Cases: Serotype 1 Grade II	2	0		
Episodes: Serotype 1 Grade II	2	0		
Cases: Serotype 1 Grade III	2	0		
Episodes: Serotype 1 Grade III	2	0		
Cases: Serotype 1 Grade IV	0	0		
Episodes: Serotype 1 Grade IV	0	0		
Cases: Serotype 2 Any grade	1	1		
Episodes: Serotype 2 Any grade	1	1		
Cases: Serotype 2 Grade I	1	1		
Episodes: Serotype 2 Grade I	1	1		
Cases: Serotype 2 Grade II	0	0		
Episodes: Serotype 2 Grade II	0	0		
Cases: Serotype 2 Grade III	0	0		
Episodes: Serotype 2 Grade III	0	0		
Cases: Serotype 2 Grade IV	0	0		
Episodes: Serotype 2 Grade IV	0	0		
Cases: Serotype 3 Any grade	1	0		
Episodes: Serotype 3 Any grade	1	0		
Cases: Serotype 3 Grade I	0	0		
Episodes: Serotype 3 Grade I	0	0		
Cases: Serotype 3 Grade II	1	0		
Episodes: Serotype 3 Grade II	1	0		
Cases: Serotype 3 Grade III	0	0		
Episodes: Serotype 3 Grade III	0	0		
Cases: Serotype 3 Grade IV	0	0		
Episodes: Serotype 3 Grade IV	0	0		
Cases: Serotype 4 Any grade	1	2		
Episodes: Serotype 4 Any grade	1	2		
Cases: Serotype 4 Grade I	0	1		
Episodes: Serotype 4 Grade I	0	1		
Cases: Serotype 4 Grade II	1	1		
Episodes: Serotype 4 Grade II	1	1		
Cases: Serotype 4 Grade III	0	0		
Episodes: Serotype 4 Grade III	0	0		
Cases: Serotype 4 Grade IV	0	0		
Episodes: Serotype 4 Grade IV	0	0		
Cases: Unserotyped Any grade	0	0		
Episodes: Unserotyped Any grade	0	0		
Cases: Unserotyped Grade I	0	0		
Episodes: Unserotyped Grade I	0	0		
Cases: Unserotyped Grade II	0	0		

Episodes: Unserotyped Grade II	0	0		
Cases: Unserotyped Grade III	0	0		
Episodes: Unserotyped Grade III	0	0		
Cases: Unserotyped Grade IV	0	0		
Episodes: Unserotyped Grade IV	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Throughout the study period (Year 1 to Year 4)

Adverse event reporting additional description:

This study involved a passive surveillance of hospitalized dengue cases and related and fatal SAEs in subjects that participated in a previous study. Non-serious adverse event data was not collected since no vaccine was administered in the present study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	Control Group

Reporting group description:

Subjects received either Rabies vaccine (Verorab®) or placebo control as a first injection on Day 0, placebo for second and third injections at 6 and 12 months, respectively, in the original CYD23 study.

Reporting group title	CYD Dengue Vaccine Group

Reporting group description:

Subjects received 3 injections of CYD dengue vaccine, 1 injection each at 0, 6, and 12 months in study CYD23.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: This was a long-term immunogenicity follow-up study of subjects who participated in the primary study. No vaccines were administered in the follow-up study and non-SAE data was also not collected.

Serious adverse events	Control Group	CYD Dengue Vaccine Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 1072 (0.19%)	3 / 2131 (0.14%)	
number of deaths (all causes)	2	3	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Gun-shot wound			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 1072 (0.00%)	2 / 2131 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Road traffic accident			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 1072 (0.09%)	1 / 2131 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	

General disorders and administration site conditions			
Drowning			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 1072 (0.09%)	0 / 2131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Control Group	CYD Dengue Vaccine Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1072 (0.00%)	0 / 2131 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 January 2014	Additional clarifications were added to the study objectives.
17 February 2014	Study objectives were further updated and statistical analyses were revised.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/22975340