Clinical trial results:
Efficacy and Safety of a Novel Tetravalent Dengue Vaccine in Healthy Children and Adolescents Aged 9 to 16 Years in Latin America

Summary

EudraCT number	2014-001716-19
Trial protocol	Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1
This version publication date	08 February 2016
First version publication date	02 August 2015

Trial information

Trial identification

Sponsor protocol code	CYD15

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01374516
WHO universal trial number (UTN)	U1111-1116-4986

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur SA
Sponsor organisation address	2, avenue Pont Pasteur, Lyon Cedex 07, France, 69367
Public contact	Senior Director, Clinical Development, Sanofi Pasteur SA, 33 4 37 65 60 60, eric.plennevaux@sanofipasteur.com
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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	Interim
Date of interim/final analysis	09 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2014
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy of CYD dengue vaccine after 3 vaccinations (one each at 0, 6 and 12 months) in preventing symptomatic virologically-confirmed dengue cases, regardless of the severity, due to any of the four serotypes

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	08 June 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	47 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Colombia: 9743
Country: Number of subjects enrolled	Honduras: 2799
Country: Number of subjects enrolled	Brazil: 3548
Country: Number of subjects enrolled	Mexico: 3464
Country: Number of subjects enrolled	Puerto Rico: 1315
Worldwide total number of subjects	20869
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)	9458
Adolescents (12-17 years)	11411
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 from 08 June 2011 to 16 March 2012 at 5 clinical sites in Brazil, 9 in Colombia, 1 in Honduras, 5 in Mexico, and 2 in Puerto Rico.

Pre-assignment

Screening details:

A total of 20869 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:

The observer-blind design was chosen since the products have different aspects and could be recognized. The person who performed vaccinations knew which product was administered while neither the subject nor the Investigator in charge of safety evaluation knew which product was injected. To maintain the blind and minimize any potential bias, the control group used the same route and schedule as the study vaccine.

Arms

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

Arm description:

Subjects received 3 injections of the CYD Dengue vaccine, 1 injection each at 0, 6 months, and 12 months.

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, 3 injections. One each at 0, 6, and 12 months.

Arm title	Control group

Arm description:

Subjects received 3 injections of placebo, 1 injection each at 0, 6, and 12 months.

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, 3 injections. One each at 0, 6, and 12 months.

Number of subjects in period 1	CYD Dengue vaccine group	Control group
Started	13920	6949
Completed	13281	6640
Not completed	639	309
Consent withdrawn by subject	480	240
Adverse event, non-fatal	3	-
Serious adverse event	7	9
Lost to follow-up	106	46
Protocol deviation	43	14

Baseline characteristics

Reporting groups	
Reporting group title	CYD Dengue vaccine group
Reporting group description:	
Subjects received 3 injections of the CYD Dengue vaccine, 1 injection each at 0, 6 months, and 12 months.	
Reporting group title	Control group
Reporting group description:	
Subjects received 3 injections of placebo, 1 injection each at 0, 6, and 12 months.	

Reporting group values	CYD Dengue vaccine group	Control group	Total
Number of subjects	13920	6949	20869
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)	6307	3151	9458
Adolescents (12-17 years)	7613	3798	11411
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	12.5	12.5	
standard deviation	± 2.14	± 2.13	-
Gender categorical Units: Subjects			
Female	7042	3531	10573
Male	6878	3418	10296

End points

End points reporting groups

Reporting group title	CYD Dengue vaccine group
Reporting group description:	
Subjects received 3 injections of the CYD Dengue vaccine, 1 injection each at 0, 6 months, and 12 months.	
Reporting group title	Control group
Reporting group description:	
Subjects received 3 injections of placebo, 1 injection each at 0, 6, and 12 months.	

Primary: Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases During the Active Phase Post-dose 3 Injection with CYD Dengue Vaccine

End point title	Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases During the Active Phase Post-dose 3 Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue (VCD) cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction (RT-PCR) and/or dengue NS1 enzyme-linked immunosorbent assay (ELISA).
Cases: number of subjects with at least one symptomatic VCD episode from 28 days post-injection 3 to the end of the Active Phase.
Vaccine efficacy was reported as density incidence (cases/100 person-years at risk). The person-years at risk was the cumulative time (in years) until the subject was diagnosed with VCD or until the end of the active period, whichever came first.
Density incidence: number of VCD cases divided by the cumulative person-years at risk. The vaccine efficacy is considered significant if the lower bound of its 95% CI was greater than 25%.

End point type	Primary

End point timeframe:

28 days post-injection 3 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12574	6261		
Units: Cases				
number (not applicable)				
Symptomatic virologically-confirmed dengue cases	176	221		
Person-years at risk	11793	5809		
Density incidence	1.5	3.8		

Statistical analyses

Statistical analysis title	Vaccine efficacy of the CYD dengue vaccine

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases

in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	18835
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	60.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	52
upper limit	68

Primary: Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to Any and Each Serotype Post-dose 3 Injection with CYD Dengue Vaccine

End point title	Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to Any and Each Serotype Post-dose 3 Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue (VCD) cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction (RT-PCR) and/or dengue NS1 enzyme-linked immunosorbent assay (ELISA).
Outcome assessed in modified full analysis set for efficacy.
Cases: number of subjects with at least one symptomatic VCD episode from 28 days post-injection 3 to the end of the Active Phase.
Vaccine efficacy was reported as density incidence (cases/100 person-years at risk). The person-years at risk was the cumulative time (in years) until the subject was diagnosed with VCD or until the end of the active period, whichever came first.
Density incidence: number of VCD cases divided by the cumulative person-years at risk. The vaccine efficacy is considered significant if the lower bound of its 95% CI was greater than 25%.

End point type	Primary

End point timeframe:

28 days post-injection 3 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13288	6643		
Units: Cases				
number (not applicable)				
Cases; Due to any of the 4 serotypes	185	236		
Cases; Serotype 1	66	66		
Cases; Serotype 2	58	50		
Cases; Serotype 3	43	82		
Cases; Serotype 4	18	40		
Cases; Unserotyped	6	3		
Person-years at risk;Due to any of the 4 serotypes	12458	6157		
Person-years at risk; Serotype 1	12478	6196		

Person-years at risk; Serotype 2	12495	6219		
Person-years at risk; Serotype 3	12514	6213		
Person-years at risk; Serotype 4	12522	6206		
Person-years at risk; Unserotyped	12540	6268		
Density incidence; Due to any of the 4 serotypes	1.5	3.8		
Density incidence; Serotype 1	0.5	1.1		
Density incidence; Serotype 2	0.5	0.8		
Density incidence; Serotype 3	0.3	1.3		
Density incidence; Serotype 4	0.1	0.6		
Density incidence; Unserotyped	0.1	0.1		

Statistical analyses

Statistical analysis title	Vaccine efficacy of CYD dengue (Any serotype)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%. The point estimate (CI) reported corresponds to the vaccine efficacy due to any of the 4 serotypes.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	61.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	52.8
upper limit	68.2

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 1)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%. The point estimate (CI) reported corresponds to the vaccine efficacy of Serotype 1.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	50.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	29.1
upper limit	65.2

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 2)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%. The point estimate (CI) reported corresponds to the vaccine efficacy of Serotype 2.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	42.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	14
upper limit	61.1

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 3)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%. The point estimate (CI) reported corresponds to the vaccine efficacy of Serotype 3.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	74
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.9
upper limit	82.4

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 4)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%. The point estimate (CI) reported corresponds to the vaccine efficacy of Serotype 4.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	77.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	60.2
upper limit	88

Statistical analysis title	Vaccine efficacy of CYD dengue (Unserotyped)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%. The point estimate (CI) reported corresponds to the vaccine efficacy of unserotyped.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-517.8
upper limit	78.6

Secondary: Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to At Least Three Serotypes Post-dose 3 Injection with CYD Dengue Vaccine

End point title	Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to At Least Three Serotypes Post-dose 3 Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue (VCD) cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction (RT-PCR) and/or dengue NS1 enzyme-linked immunosorbent assay (ELISA). Cases: number of subjects with at least one symptomatic VCD episode from 28 days post-injection 3 to the end of the Active Phase.
Vaccine efficacy was reported as density incidence (cases/100 person-years at risk). The person-years at risk was the cumulative time (in years) until the subject was diagnosed with VCD or until the end of

the active period, whichever came first.
Density incidence: number of VCD cases divided by the cumulative person-years at risk. The vaccine efficacy is considered significant if the lower bound of its 95% CI was greater than 25%.

End point type	Secondary

End point timeframe:

28 days post-injection 3 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13288	6643		
Units: Cases				
number (not applicable)				
Cases; Serotypes 1 or 2 or 3	161	193		
Cases; Serotypes 1 or 2 or 4	139	154		
Cases; Serotypes 2 or 3 or 4	118	171		
Cases; Serotypes 1 or 3 or 4	125	186		
Person-years at risk; Serotypes 1 or 2 or 3	12470	6183		
Person-years at risk; Serotypes 1 or 2 or 4	12477	6194		
Person-years at risk; Serotypes 2 or 3 or 4	12492	6189		
Person-years at risk; Serotypes 1 or 3 or 4	12481	6177		
Density incidence; Serotypes 1 or 2 or 3	1.3	3.1		
Density incidence; Serotypes 1 or 2 or 4	1.1	2.5		
Density incidence; Serotypes 2 or 3 or 4	0.9	2.8		
Density incidence; Serotypes 1 or 3 or 4	1	3		

Statistical analyses

Statistical analysis title	Vaccine efficacy; Serotype 1 or 2 or 3

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	58.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	48.7
upper limit	66.7

Statistical analysis title	Vaccine efficacy; Serotype 1 or 2 or 4

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	55.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	43.3
upper limit	64.6

Statistical analysis title	Vaccine efficacy; Serotype 2 or 3 or 4

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	65.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	56.5
upper limit	73.2

Statistical analysis title	Vaccine efficacy; Serotype 1 or 3 or 4

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	Control group v CYD Dengue vaccine group

Number of subjects included in analysis	19931
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	66.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.1
upper limit	73.7

Secondary: Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases During the Active Phase Injection with CYD Dengue Vaccine

End point title	Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases During the Active Phase Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue (VCD) cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction (RT-PCR) and/or dengue NS1 enzyme-linked immunosorbent assay (ELISA). Outcome assessed in full analysis set for efficacy.
Cases: number of subjects with at least one symptomatic VCD episode from Day 0 to the end of the Active Phase.
Vaccine efficacy was reported as density incidence (cases/100 person-years at risk). The person-years at risk was the cumulative time (in years) until the subject was diagnosed with VCD or until the end of the active period, whichever came first.
Density incidence: number of VCD cases divided by the cumulative person-years at risk. The vaccine efficacy is considered significant if the lower bound of its 95% CI was greater than 25%.

End point type	Secondary

End point timeframe:

Day 0 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13914	6940		
Units: Cases				
number (not applicable)				
Symptomatic virologically-confirmed dengue cases	277	385		
Person-years at risk	26883	13204		
Density incidence	1	2.9		

Statistical analyses

Statistical analysis title	Vaccine efficacy of CYD dengue vaccine

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the

vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	64.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.7
upper limit	69.8

Secondary: Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to Each Serotype During the Active Phase After at Least One Injection with CYD Dengue Vaccine

End point title	Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to Each Serotype During the Active Phase After at Least One Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue (VCD) cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction (RT-PCR) and/or dengue NS1 enzyme-linked immunosorbent assay (ELISA).
Cases: number of subjects with at least one symptomatic VCD episode from Day 0 to the end of the Active Phase.
Vaccine efficacy was reported as density incidence (cases/100 person-years at risk). The person-years at risk was the cumulative time (in years) until the subject was diagnosed with VCD or until the end of the active period, whichever came first.
Density incidence: number of VCD cases divided by the cumulative person-years at risk. The vaccine efficacy is considered significant if the lower bound of its 95% CI was greater than 25%.

End point type	Secondary

End point timeframe:

Day 0 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13914	6940		
Units: Cases				
number (not applicable)				
Cases; Serotype 1	99	109		
Cases; Serotype 2	84	84		
Cases; Serotype 3	55	106		
Cases; Serotype 4	32	83		
Cases; Unserotyped	15	14		
Person-years at risk; Serotype 1	27016	13434		
Person-years at risk; Serotype 2	27035	13461		
Person-years at risk; Serotype 3	27060	13459		
Person-years at risk; Serotype 4	27063	13442		

Person-years at risk; Unserotyped	27079	13514		
Density incidence; Serotype 1	0.4	0.8		
Density incidence; Serotype 2	0.3	0.6		
Density incidence; Serotype 3	0.2	0.8		
Density incidence; Serotype 4	0.1	0.6		
Density incidence; Unserotyped	0.1	0.1		

Statistical analyses

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 1)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	54.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	40.2
upper limit	65.9

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 2)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	50.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.8
upper limit	63.6

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 3)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	74.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	63.9
upper limit	81.7

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 4)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	Control group v CYD Dengue vaccine group
Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	80.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	70.9
upper limit	87.7

Statistical analysis title	Vaccine efficacy of CYD dengue (Unserotyped)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group

Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	46.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.6
upper limit	75.9

Secondary: Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases During the Active Phase Post-dose 2 Injection with CYD Dengue Vaccine

End point title	Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases During the Active Phase Post-dose 2 Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue (VCD) cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction (RT-PCR) and/or dengue NS1 enzyme-linked immunosorbent assay (ELISA).
Cases: number of subjects with at least one symptomatic VCD episode from 28 days post-injection 2 to the end of the Active Phase.
Vaccine efficacy was reported as density incidence (cases/100 person-years at risk). The person-years at risk was the cumulative time (in years) until the subject was diagnosed with VCD or until the end of the active period, whichever came first.
Density incidence: number of VCD cases divided by the cumulative person-years at risk. The vaccine efficacy is considered significant if the lower bound of its 95% CI was greater than 25%.

End point type	Secondary

End point timeframe:

28 days post-injection 2 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13506	6765		
Units: Cases				
number (not applicable)				
Symptomatic virologically-confirmed dengue cases	236	306		
Person-years at risk	19133	9443		
Density incidence	1.2	3.2		

Statistical analyses

Statistical analysis title	Vaccine efficacy of CYD dengue vaccine

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases

in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	61.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	54.7
upper limit	68

Secondary: Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to Any and Each Serotype Post-dose 2 Injection with CYD Dengue Vaccine

End point title	Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to Any and Each Serotype Post-dose 2 Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue (VCD) cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction (RT-PCR) and/or dengue NS1 enzyme-linked immunosorbent assay (ELISA). Outcome in Other Efficacy Analysis Set.
Cases: number of subjects with at least one symptomatic VCD episode from 28 days post-injection 2 to the end of the Active Phase.
Vaccine efficacy was reported as density incidence (cases/100 person-years at risk). The person-years at risk was the cumulative time (in years) until the subject was diagnosed with VCD or until the end of the active period, whichever came first.
Density incidence: number of VCD cases divided by the cumulative person-years at risk. The vaccine efficacy is considered significant if the lower bound of its 95% CI was greater than 25%.

End point type	Secondary

End point timeframe:

28 days post-injection 2 to the end of the Active Phase.

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13506	6765		
Units: Cases				
number (not applicable)				
Cases; Serotype 1	86	87		
Cases; Serotype 2	73	67		
Cases; Serotype 3	50	93		
Cases; Serotype 4	20	55		
Cases; Unserotyped	14	13		
Person-years at risk; Serotype 1	19203	9551		
Person-years at risk; Serotype 2	19222	9577		
Person-years at risk; Serotype 3	19245	9574		
Person-years at risk; Serotype 4	19250	9558		

Person-years at risk; Unserotyped	19265	9267		
Density incidence; Serotype 1	0.4	0.9		
Density incidence; Serotype 2	0.4	0.7		
Density incidence; Serotype 3	0.3	1		
Density incidence; Serotype 4	0.1	0.6		
Density incidence; Unserotyped	0.1	0.1		

Statistical analyses

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 1)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	50.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	33
upper limit	63.9

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 2)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	45.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.2
upper limit	61.6

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 3)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	73.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.9
upper limit	81.4

Statistical analysis title	Vaccine efficacy of CYD dengue (Serotype 4)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	81.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	69.4
upper limit	89.8

Statistical analysis title	Vaccine efficacy of CYD dengue (Unserotyped)

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	46.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.3
upper limit	76.5

Secondary: Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to At Least Three Serotypes Post-dose 2 Injection with CYD Dengue Vaccine

End point title	Vaccine Efficacy Against Symptomatic Virologically-confirmed Dengue Cases Due to At Least Three Serotypes Post-dose 2 Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue (VCD) cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction (RT-PCR) and/or dengue NS1 enzyme-linked immunosorbent assay (ELISA). Outcome assessed in the Other Efficacy Analysis Set.
Cases: number of subjects with at least one symptomatic VCD episode from 28 days post-injection 2 to the end of the Active Phase.
Vaccine efficacy was reported as density incidence (cases/100 person-years at risk). The person-years at risk was the cumulative time (in years) until the subject was diagnosed with VCD or until the end of the active period, whichever came first.
Density incidence: number of VCD cases divided by the cumulative person-years at risk. The vaccine efficacy is considered significant if the lower bound of its 95% CI was greater than 25%.

End point type	Secondary

End point timeframe:

28 days post-injection 2 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13506	6765		
Units: Cases				
number (not applicable)				
Cases; Serotype 1 or 2 or 3	202	240		
Cases; Serotype 1 or 2 or 4	175	206		
Cases; Serotype 2 or 3 or 4	142	214		
Cases; Serotype 1 or 3 or 4	154	232		
Person-years at risk; Serotype 1 or 2 or 3	19157	9498		
Person-years at risk; Serotype 1 or 2 or 4	19170	9503		
Person-years at risk; Serotype 2 or 3 or 4	19199	9509		
Person-years at risk; Serotype 1 or 3 or 4	19183	9494		
Density incidence; Serotype 1 or 2 or 3	1.1	2.5		
Density incidence; Serotype 1 or 2 or 4	0.9	2.2		
Density incidence; Serotype 2 or 3 or 4	0.7	2.3		
Density incidence; Serotype 1 or 3 or 4	0.8	2.4		

Statistical analyses

Statistical analysis title	Vaccine efficacy; Serotype 1 or 2 or 3

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	58.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	49.5
upper limit	65.6

Statistical analysis title	Vaccine efficacy; Serotype 1 or 2 or 4

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	57.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	48.2
upper limit	65.8

Statistical analysis title	Vaccine efficacy; Serotype 2 or 3 or 4

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases

in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	67.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	59.2
upper limit	73.6

Statistical analysis title	Vaccine efficacy; Serotype 1 or 3 or 4

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20271
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	67.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	59.6
upper limit	73.4

Secondary: Number of Subjects With at Least One Symptomatic Virologically-confirmed Dengue Case Meeting DHF WHO Criteria During the Active Phase Due to Any and Each Serotype Post Injection with CYD Dengue Vaccine

End point title	Number of Subjects With at Least One Symptomatic Virologically-confirmed Dengue Case Meeting DHF WHO Criteria During the Active Phase Due to Any and Each Serotype Post Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue cases were defined by dengue hemorrhagic fever (DHF) World Health Organization (WHO) as temperature ≥38°C lasting 2 to 7 days, hemorrhagic manifestations, thrombocytopenia, and plasma leakage and confirmed by dengue RT-PCR and/or dengue NS1 ELISA. DHF WHO cases were subjects with at least one symptomatic virologically-confirmed dengue episode meeting DHF WHO criteria from Day 0 to the end of the Active Phase (13 months post-injection 3). DHF Grade I, Fever with non-specific constitutional symptoms and positive tourniquet test as hemorrhagic manifestation; Grade II, Spontaneous bleeding plus Grade I manifestations, usually in the form of skin and/or hemorrhages; Grade III, Circulatory failure manifested by rapid and weak pulse, narrowing of pulse pressure (≤20 mmHg) or hypotension, with clammy skin and restlessness; Grade IV, profound shock with undetectable blood pressure and pulse.

End point type	Secondary

End point timeframe:

Day 0 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13914	6940		
Units: Number of subjects				
number (not applicable)				
Due to any of the 4 serotypes; Any grade	1	10		
Due to any of the 4 serotypes; Grade I	0	2		
Due to any of the 4 serotypes; Grade II	1	8		
Due to any of the 4 serotypes; Grade III	0	0		
Due to any of the 4 serotypes; Grade IV	0	0		
Serotype 1; Any grade	1	3		
Serotype 2; Any grade	0	3		
Serotype 3; Any grade	0	3		
Serotype 4; Any grade	0	1		
Unserotyped; Any grade	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: The Ratio Convalescent/Acute IgM and IgG ELISA Results for All Suspected Dengue Cases During the Active Phase Due to Any and Each Serotype Post Injection with CYD Dengue Vaccine

End point title	The Ratio Convalescent/Acute IgM and IgG ELISA Results for All Suspected Dengue Cases During the Active Phase Due to Any and Each Serotype Post Injection with CYD Dengue Vaccine

End point description:

The ratio of convalescent/acute is computed if acute and convalescent values are > 0. The ratios of virologically-confirmed dengue (VCD) and non-VCD cases are reported for IgM and IgG.

End point type	Secondary

End point timeframe:

Day 0 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	252	328		
Units: Ratio (Convalescent/Acute)				
arithmetic mean (confidence interval 95%)				

IgM; VCD	8 (6.72 to 9.28)	9.81 (8.47 to 11.1)		
IgM; Non-VCD	1.06 (1.03 to 1.08)	1.07 (1.03 to 1.1)		
IgG; VCD	2.16 (1.91 to 2.41)	4.96 (4.1 to 5.82)		
IgG; Non-VCD	1.05 (1.04 to 1.06)	1.17 (1.11 to 1.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects By Country with at Least One Symptomatic Virologically-confirmed Dengue Case Due to Any Serotype During the Active Phase and Post-dose 3 Injection with CYD Dengue Vaccine

End point title	Number of Subjects By Country with at Least One Symptomatic Virologically-confirmed Dengue Case Due to Any Serotype During the Active Phase and Post-dose 3 Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction and/or dengue NS1 enzyme-linked immunosorbent assay. Cases were defined as the number of subjects with at least one symptomatic virologically-confirmed dengue episode from 28 days post-injection 3 to the end of Active Phase (post-dose 3) or during the Active Phase.

End point type	Secondary

End point timeframe:

28 days post-injection 3 to the Active Phase (post-dose 3) or during the Active Phase

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13920	6949		
Units: Number of subjects				
number (not applicable)				
Active phase; Brazil	38	81		
Active phase; Colombia	108	164		
Active phase; Honduras	42	71		
Active phase; Mexico	78	56		
Active phase; Puerto Rico	11	13		
Post-dose 3; Brazil	14	33		
Post-dose 3; Colombia	74	108		
Post-dose 3; Honduras	37	59		
Post-dose 3; Mexico	51	28		
Post-dose 3; Puerto Rico	9	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaccine Efficacy By Country Against Symptomatic Virologically-confirmed Dengue Case During the Active Phase and Post-dose 3 Injection with CYD Dengue Vaccine

End point title	Vaccine Efficacy By Country Against Symptomatic Virologically-confirmed Dengue Case During the Active Phase and Post-dose 3 Injection with CYD Dengue Vaccine

End point description:

Symptomatic virologically-confirmed dengue cases were defined as acute febrile illness (temperature ≥38°C on at least 2 consecutive days) and confirmed by dengue reverse transcriptase-polymerase chain reaction and/or dengue NS1 enzyme-linked immunosorbent assay. Vaccine efficacy was reported as density incidence (cases/100 person-years at risk). Density incidence was calculated as the number of virologically-confirmed dengue cases divided by the cumulative person-years at risk, where the person-years at risk was defined as the sum of individual units of time for which the subjects contributed to the analyses.

End point type	Secondary

End point timeframe:

28 days post-injection 3 to the Active Phase (post-dose 3) or during the Active Phase

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13920	6949		
Units: Density incidence				
number (confidence interval 95%)				
Active phase; Brazil	0.8 (0.6 to 1.1)	3.7 (2.9 to 4.6)		
Active phase; Colombia	0.9 (0.7 to 1)	2.7 (2.3 to 3.1)		
Active phase; Honduras	1.2 (0.8 to 1.6)	4 (3.2 to 5)		
Active phase; Mexico	1.7 (1.4 to 2.1)	2.5 (1.9 to 3.2)		
Active phase; Puerto Rico	0.7 (0.3 to 1.2)	1.6 (0.8 to 2.6)		
Post-dose 3; Brazil	0.7 (0.4 to 1.1)	3.3 (2.2 to 4.5)		
Post-dose 3; Colombia	1.3 (1 to 1.6)	3.8 (3.1 to 4.5)		
Post-dose 3; Honduras	2.2 (1.5 to 3)	7.2 (5.5 to 9.1)		
Post-dose 3; Mexico	2.4 (1.8 to 3.1)	2.6 (1.8 to 3.8)		
Post-dose 3; Puerto Rico	1.2 (0.5 to 2.2)	2.1 (0.9 to 4.1)		

Statistical analyses

Statistical analysis title	Vaccine efficacy; Active phase; Brazil

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group

Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	77.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	66.5
upper limit	85.1

Statistical analysis title	Vaccine efficacy; Active phase; Colombia

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	Control group v CYD Dengue vaccine group
Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	67.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.3
upper limit	74.7

Statistical analysis title	Vaccine efficacy; Active phase; Honduras

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	71.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	57
upper limit	80.7

Statistical analysis title	Vaccine efficacy; Active phase; Mexico

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	31.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	51.9

Statistical analysis title	Vaccine efficacy; Active phase; Puerto Rico

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	57.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	82.8

Statistical analysis title	Vaccine efficacy; Post-dose 3; Brazil

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group

Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	79.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	60.4
upper limit	89.8

Statistical analysis title	Vaccine efficacy; Post-dose 3; Colombia

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	66
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.9
upper limit	75.1

Statistical analysis title	Vaccine efficacy; Post-dose 3; Honduras

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	69.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.3
upper limit	80.4

Statistical analysis title	Vaccine efficacy; Post-dose 3; Mexico

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	8.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.3
upper limit	43.5

Statistical analysis title	Vaccine efficacy; Post-dose 3; Puerto Rico

Statistical analysis description:

The statistical methodology was based on the use of the two-sided 95% confidence interval (CI) of the vaccine efficacy. The CI was calculated using the exact method conditional on the total number of cases in both groups. The vaccine efficacy of the CYD dengue vaccine was considered significant if the lower bound of its 95% CI was greater than 25%.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20869
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Vaccine efficacy (%)
Point estimate	43.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.5
upper limit	80.6

Secondary: Incidence of Hospitalized Virologically-confirmed Dengue By Country During the Active Phase Due to Any Serotype Post-injection with CYD Dengue Vaccine

End point title	Incidence of Hospitalized Virologically-confirmed Dengue By Country During the Active Phase Due to Any Serotype Post-injection with CYD Dengue Vaccine

End point description:

Cases were defined as the number of subjects with at least one hospitalized virologically-confirmed dengue episode, where episodes were defined as the number of hospitalized virologically-confirmed dengue episodes. The annual incidence rate is reported and was calculated based on the cases among

the subjects present at the beginning of each year or mean of number of subjects followed during the years included in the considered period x 100 converted in annual rate.

End point type	Secondary

End point timeframe:

Day 0 to the end of the Active Phase (13 months post-injection 3)

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13915	6939		
Units: Incidence				
number (confidence interval 95%)				
Brazil	0.1 (0 to 0.1)	0.2 (0 to 0.4)		
Colombia	0.1 (0 to 0.1)	0.4 (0.3 to 0.6)		
Honduras	0.1 (0 to 0.3)	0.4 (0.1 to 0.8)		
Mexico	0.1 (0 to 0.2)	0.1 (0 to 0.4)		
Puerto Rico	0.1 (0 to 0.4)	0.1 (0 to 0.6)		

Statistical analyses

Statistical analysis title	Incidence of hospitalized dengue; Brazil

Statistical analysis description:

The relative risk (RR) was calculated for each country to assess the reduction of the incidence of hospitalized cases due to any serotype in subjects receiving at least 1 dose CYD dengue vaccine compared with control. A RR <1 indicates a reduction in incidence in the CYD dengue vaccine group.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.124
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1.25

Statistical analysis title	Incidence of hospitalized dengue; Colombia

Statistical analysis description:

The relative risk (RR) was calculated for each country to assess the reduction of the incidence of hospitalized cases due to any serotype in subjects receiving at least 1 dose CYD dengue vaccine compared with control. A RR <1 indicates a reduction in incidence in the CYD dengue vaccine group.

Comparison groups	CYD Dengue vaccine group v Control group

Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.125
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.29

Statistical analysis title	Incidence of hospitalized dengue; Honduras

Statistical analysis description:

The relative risk (RR) was calculated for each country to assess the reduction of the incidence of hospitalized cases due to any serotype in subjects receiving at least 1 dose CYD dengue vaccine compared with control. A RR <1 indicates a reduction in incidence in the CYD dengue vaccine group.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.285
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	1.12

Statistical analysis title	Incidence of hospitalized dengue; Mexico

Statistical analysis description:

The relative risk (RR) was calculated for each country to assess the reduction of the incidence of hospitalized cases due to any serotype in subjects receiving at least 1 dose CYD dengue vaccine compared with control. A RR <1 indicates a reduction in incidence in the CYD dengue vaccine group.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	0.498
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	3.72

Statistical analysis title	Incidence of hospitalized dengue; Puerto Rico

Statistical analysis description:

The relative risk (RR) was calculated for each country to assess the reduction of the incidence of hospitalized cases due to any serotype in subjects receiving at least 1 dose CYD dengue vaccine compared with control. A RR <1 indicates a reduction in incidence in the CYD dengue vaccine group.

Comparison groups	CYD Dengue vaccine group v Control group
Number of subjects included in analysis	20854
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk ratio (RR)
Point estimate	1.009
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	59.55

Secondary: Percentage of Subjects with Antibody Titer ≥ 10 (1/dil) Against Each Serotype with the Parental Dengue Virus Strains Before and Post-injection with CYD Dengue Tetravalent Vaccine

End point title	Percentage of Subjects with Antibody Titer ≥ 10 (1/dil) Against Each Serotype with the Parental Dengue Virus Strains Before and Post-injection with CYD Dengue Tetravalent Vaccine

End point description:

Dengue neutralizing antibody levels were measured by the plaque reduction neutralization test (PRNT).

End point type	Secondary

End point timeframe:

Pre-Injection 1 and Post-Injection 2, Post-Injection 3, and 1 year follow up Post-Injection 3

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1301	643		
Units: Percentage of subjects				
number (not applicable)				
Serotype 1; Pre-Injection 1	72.8	70.5		
Serotype 1; Post-Injection 2	92.7	71.8		
Serotype 1; Post-Injection 3	94.9	74.2		
Serotype 1; 1 year follow up Post-Injection 3	85.6	73.6		
Serotype 2; Pre-Injection 1	76.1	73.8		
Serotype 2; Post-Injection 2	97.5	75.1		
Serotype 2; Post-Injection 3	98.5	77.2		
Serotype 2; 1 year follow up Post-Injection 3	94.1	78.8		
Serotype 3; Pre-Injection 1	76.5	73.6		
Serotype 3; Post-Injection 2	98.5	75.7		
Serotype 3; Post-Injection 3	98.4	78		

Serotype 3; 1 year follow up Post-Injection 3	92.7	76.1		
Serotype 4; Pre-Injection 1	68.2	65		
Serotype 4; Post-Injection 2	96.9	67		
Serotype 4; Post-Injection 3	98.1	68.9		
Serotype 4; 1 year follow up Post-Injection 3	94.9	68.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Antibody Titer ≥ 10 (1/dil) Against At Least 1, 2, 3, or 4 Serotypes with the Parental Dengue Virus Strains Before and Post-injection with CYD Dengue Tetravalent Vaccine

End point title	Percentage of Subjects with Antibody Titer ≥ 10 (1/dil) Against At Least 1, 2, 3, or 4 Serotypes with the Parental Dengue Virus Strains Before and Post-injection with CYD Dengue Tetravalent Vaccine

End point description:

Dengue neutralizing antibody levels were measured by the plaque reduction neutralization test (PRNT).

End point type	Secondary

End point timeframe:

Pre-Injection 1 and Post-Injection 2, Post-Injection 3, and 1 year follow up Post-Injection 3

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1301	643		
Units: Percentage of subjects				
number (not applicable)				
At least 1 serotype; Pre-Injection 1	80.6	77.2		
At least 1 serotype; Post-Injection 2	99.8	80.8		
At least 1 serotype; Post-Injection 3	99.8	84.1		
At least 1 serotype; 1 yr follow up Post-Inj. 3	99	81.2		
At least 2 serotypes; Pre-Injection 1	75.6	73.5		
At least 2 serotypes; Post-Injection 2	98.8	74.6		
At least 2 serotypes; Post-Injection 3	99.5	76.9		
At least 2 serotypes; 1 yr follow up Post-Inj. 3	95.3	77.2		
At least 3 serotypes; Pre-Injection 1	72.7	70.7		
At least 3 serotypes; Post-Injection 2	96.5	71.8		
At least 3 serotypes; Post-Injection 3	98.1	73		
At least 3 serotypes; 1 yr follow up Post-Inj. 3	90.4	74		
All 4 serotypes; Pre-Injection 1	64.3	61		
All 4 serotypes; Post-Injection 2	90.4	62.1		
All 4 serotypes; Post-Injection 3	92.6	64.4		

All 4 serotypes; 1 yr follow up Post-Inj. 3	81.8	64.5		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects with Solicited Injection-site and Systemic Reactions Following Each Injection with CYD Dengue Tetravalent Vaccine

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 (9-11 years): Pain, Incapacitating, unable to perform usual activities; Erythema and Swelling, ≥50 mm. Grade 3 Solicited injection site reactions (12-16 years): Pain, Significant, prevents daily activity; Erythema and Swelling, >100 mm. Grade 3 Solicited injection site reactions: Fever, ≥39°C; Headache, Malaise, Myalgia, and Asthenia, Significant, prevents daily activity.

End point type	Secondary

End point timeframe:

Day 0 up to Day 14 post-each injection

End point values	CYD Dengue vaccine group	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1326	657		
Units: Percentage of subjects				
number (not applicable)				
Injection site Pain; Post-Injection 1	32.4	26.3		
Injection site Pain; Post-Injection 2	25.6	16.4		
Injection site Pain; Post-Injection 3	22.5	16.5		
Grade 3 Injection site Pain; Post-Injection 1	0.8	0.9		
Grade 3 Injection site Pain; Post-Injection 2	0.5	0		
Grade 3 Injection site Pain; Post-Injection 3	0.9	0.3		
Injection site Erythema; Post-Injection 1	4.1	4.7		
Injection site Erythema; Post-Injection 2	1.9	1.7		
Injection site Erythema; Post-Injection 3	1.5	1.6		
Grade 3 Injection site Erythema; Post-Injection 1	0	0.2		
Grade 3 Injection site Erythema; Post-Injection 2	0.1	0		
Grade 3 Injection site Erythema; Post-Injection 3	0	0		
Injection site Swelling; Post-Injection 1	3.5	2.7		
Injection site Swelling; Post-Injection 2	1.9	0.9		
Injection site Swelling; Post-Injection 3	1.6	1.3		

Grade 3 Injection site Swelling; Post-Injection 1	0	0.2		
Grade 3 Injection site Swelling; Post-Injection 2	0	0		
Grade 3 Injection site Swelling; Post-Injection 3	0	0		
Fever; Post-Injection 1	6.8	6.6		
Fever; Post-Injection 2	5.9	7.1		
Fever; Post-Injection 3	7.3	8.7		
Grade 3 Fever; Post-Injection 1	1.7	1.1		
Grade 3 Fever; Post-Injection 2	0.8	1.2		
Grade 3 Fever; Post-Injection 3	1.1	0.8		
Headache; Post-Injection 1	39.9	41.6		
Headache; Post-Injection 2	29.8	28.5		
Headache; Post-Injection 3	29.6	25		
Grade 3 Headache; Post-Injection 1	5.1	4.1		
Grade 3 Headache; Post-Injection 2	2.1	2.3		
Grade 3 Headache; Post-Injection 3	2.6	1.9		
Malaise; Post-Injection 1	24.5	25.9		
Malaise; Post-Injection 2	20.8	16.6		
Malaise; Post-Injection 3	19.3	15.2		
Grade 3 Malaise; Post-Injection 1	2.4	2.3		
Grade 3 Malaise; Post-Injection 2	1.3	1.3		
Grade 3 Malaise; Post-Injection 3	1.4	1.1		
Myalgia; Post-Injection 1	29.2	27.4		
Myalgia; Post-Injection 2	21	15.8		
Myalgia; Post-Injection 3	20	18.4		
Grade 3 Myalgia; Post-Injection 1	2.2	1.5		
Grade 3 Myalgia; Post-Injection 2	1.6	0.8		
Grade 3 Myalgia; Post-Injection 3	1.5	0.8		
Asthenia; Post-Injection 1	24.6	22.5		
Asthenia; Post-Injection 2	17.8	16.4		
Asthenia; Post-Injection 3	16.3	17.4		
Grade 3 Asthenia; Post-Injection 1	2.7	2.6		
Grade 3 Asthenia; Post-Injection 2	1.8	1.1		
Grade 3 Asthenia; Post-Injection 3	1.3	1.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse event data were collected from Day 0 (post-vaccination) up to 13 months post-Injection 3.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14

Reporting groups	
Reporting group title	CYD Dengue vaccine group
Reporting group description:	
Subjects received 3 injections of the CYD Dengue vaccine, 1 injection each at 0, 6 months, and 12 months.	
Reporting group title	Control group
Reporting group description:	
Subjects received 3 injections of placebo, 1 injection each at 0, 6, and 12 months.	

Serious adverse events	CYD Dengue vaccine group	Control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	565 / 13915 (4.06%)	308 / 6939 (4.44%)	
number of deaths (all causes)	6	6	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoma			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian germ cell teratoma benign			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteosarcoma metastatic			

subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Surgical and medical procedures			
Caesarean section			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgery			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	6 / 13915 (0.04%)	4 / 6939 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
False labour			
subjects affected / exposed	5 / 13915 (0.04%)	3 / 6939 (0.04%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pre-eclampsia			
subjects affected / exposed	5 / 13915 (0.04%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gestational hypertension			
subjects affected / exposed	4 / 13915 (0.03%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion			
subjects affected / exposed	3 / 13915 (0.02%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abortion spontaneous incomplete			
subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion threatened			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stillbirth			
subjects affected / exposed	2 / 13915 (0.01%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion complete			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion incomplete			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion incomplete complicated			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion missed			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous complete			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blighted ovum			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication of delivery			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature labour			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Premature rupture of membranes			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retained products of conception			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Threatened labour			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal distress syndrome			
subjects affected / exposed	0 / 13915 (0.00%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oligohydramnios			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postpartum haemorrhage			

subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolonged labour			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 13915 (0.04%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue inflammation			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drowning			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malaise			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anti-neutrophil cytoplasmic antibody positive vasculitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Food allergy			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	4 / 13915 (0.03%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Testicular torsion			
subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bartholinitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysfunctional uterine bleeding			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematocolpos			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic pain			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Varicocele			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gynaecomastia			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
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	7 / 13915 (0.05%)	8 / 6939 (0.12%)	
occurrences causally related to treatment / all	1 / 9	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthmatic crisis			
subjects affected / exposed	3 / 13915 (0.02%)	3 / 6939 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status asthmaticus			
subjects affected / exposed	2 / 13915 (0.01%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pulmonary oedema			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asphyxia			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Haemothorax			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery stenosis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar hypertrophy			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epistaxis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septum deviation			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	7 / 13915 (0.05%)	4 / 6939 (0.06%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			

subjects affected / exposed	5 / 13915 (0.04%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute psychosis			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance abuse			
subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute stress disorder			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adjustment disorder			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorexia nervosa			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety disorder			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conversion disorder			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dissociative disorder			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug abuse			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional drug misuse			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatoform disorder			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression suicidal			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional self-injury			
subjects affected / exposed	0 / 13915 (0.00%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obsessive rumination			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Forearm fracture			

subjects affected / exposed	18 / 13915 (0.13%)	5 / 6939 (0.07%)	
occurrences causally related to treatment / all	0 / 18	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	9 / 13915 (0.06%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 9	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Head injury			
subjects affected / exposed	7 / 13915 (0.05%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Femur fracture			
subjects affected / exposed	5 / 13915 (0.04%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	5 / 13915 (0.04%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	5 / 13915 (0.04%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	4 / 13915 (0.03%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	4 / 13915 (0.03%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			

subjects affected / exposed	4 / 13915 (0.03%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			
subjects affected / exposed	3 / 13915 (0.02%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	3 / 13915 (0.02%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	3 / 13915 (0.02%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	3 / 13915 (0.02%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tibia fracture			
subjects affected / exposed	3 / 13915 (0.02%)	3 / 6939 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns third degree			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poisoning deliberate			

subjects affected / exposed	2 / 13915 (0.01%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tendon rupture			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal injury			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Avulsion fracture			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiphyseal fracture			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital injury			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb crushing injury			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 13915 (0.01%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue injury			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury cervical			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Stab wound			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic brain injury			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Animal bite			
subjects affected / exposed	0 / 13915 (0.00%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropod sting			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 13915 (0.00%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle injury			

subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Antepartum haemorrhage			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	9 / 13915 (0.06%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 19	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	4 / 13915 (0.03%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Convulsion			
subjects affected / exposed	3 / 13915 (0.02%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute polyneuropathy			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated migraine			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic cerebral infarction			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute disseminated encephalomyelitis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersomnia			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic generalised epilepsy			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine with aura			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenitis			

subjects affected / exposed	3 / 13915 (0.02%)	3 / 6939 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic thrombocytopenic purpora			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	10 / 13915 (0.07%)	4 / 6939 (0.06%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	5 / 13915 (0.04%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	3 / 13915 (0.02%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Inguinal hernia			
subjects affected / exposed	3 / 13915 (0.02%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 13915 (0.01%)	3 / 6939 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingivitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia, obstructive			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal functional disorder			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia, obstructive			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	3 / 13915 (0.02%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	3 / 13915 (0.02%)	4 / 6939 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder disorder			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	4 / 13915 (0.03%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Henoch-Schonlein purpura			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical urticaria			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash erythematous			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	5 / 13915 (0.04%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritic syndrome			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus nephritis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal colic			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiphysiolysis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Knee deformity			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatic fever			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sacroiliitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Juvenile arthritis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	94 / 13915 (0.68%)	52 / 6939 (0.75%)	
occurrences causally related to treatment / all	0 / 94	0 / 52	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	41 / 13915 (0.29%)	48 / 6939 (0.69%)	
occurrences causally related to treatment / all	0 / 41	0 / 48	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	32 / 13915 (0.23%)	14 / 6939 (0.20%)	
occurrences causally related to treatment / all	0 / 33	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	17 / 13915 (0.12%)	19 / 6939 (0.27%)	
occurrences causally related to treatment / all	0 / 17	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	15 / 13915 (0.11%)	12 / 6939 (0.17%)	
occurrences causally related to treatment / all	0 / 15	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	7 / 13915 (0.05%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	6 / 13915 (0.04%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 13915 (0.04%)	11 / 6939 (0.16%)	
occurrences causally related to treatment / all	0 / 6	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	5 / 13915 (0.04%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	4 / 13915 (0.03%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	3 / 13915 (0.02%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	3 / 13915 (0.02%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	3 / 13915 (0.02%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic inflammatory disease			
subjects affected / exposed	3 / 13915 (0.02%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	3 / 13915 (0.02%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	3 / 13915 (0.02%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	3 / 13915 (0.02%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	2 / 13915 (0.01%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			

subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cellulitis			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis bacterial			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis viral			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leptospirosis			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			

subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	2 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 13915 (0.01%)	3 / 6939 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	2 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebic dysentery			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chorioamnionitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis decidual			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
External ear cellulitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital infection female			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helminthic infection			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious mononucleosis			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (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	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mononucleosis syndrome			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			

subjects affected / exposed	1 / 13915 (0.01%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syphilis			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis bacterial			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhoid fever			
subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			

subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion infected			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess of salivary gland			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute tonsillitis			
subjects affected / exposed	0 / 13915 (0.00%)	2 / 6939 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebiasis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bartholin's abscess			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genitourinary tract infection			

subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mumps			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scarlet fever			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			

subjects affected / exposed	1 / 13915 (0.01%)	0 / 6939 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 13915 (0.01%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 13915 (0.00%)	1 / 6939 (0.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
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	528 / 13915 (3.79%)	273 / 6939 (3.93%)	
Nervous system disorders			
Headache			
subjects affected / exposed[1]	84 / 1333 (6.30%)	36 / 664 (5.42%)	
occurrences (all)	93	39	
Headache; Post-Injection 1			
alternative assessment type: Systematic			
subjects affected / exposed[2]	528 / 1324 (39.88%)	273 / 657 (41.55%)	
occurrences (all)	528	273	
Headache; Post-Injection 2			
alternative assessment type: Systematic			
subjects affected / exposed[3]	386 / 1297 (29.76%)	182 / 639 (28.48%)	
occurrences (all)	386	182	
Headache; Post-Injection 3			
alternative assessment type: Systematic			
subjects affected / exposed[4]	378 / 1277 (29.60%)	158 / 631 (25.04%)	
occurrences (all)	378	158	

General disorders and administration site conditions			
Injection site Pain; Post-Injection 1			
alternative assessment type: Systematic			
subjects affected / exposed[5]	430 / 1326 (32.43%)	173 / 657 (26.33%)	
occurrences (all)	430	173	
Injection site Pain; Post-Injection 2			
alternative assessment type: Systematic			
subjects affected / exposed[6]	332 / 1297 (25.60%)	105 / 639 (16.43%)	
occurrences (all)	332	105	
Injection site Pain; Post-Injection 3			
alternative assessment type: Systematic			
subjects affected / exposed[7]	288 / 1279 (22.52%)	104 / 630 (16.51%)	
occurrences (all)	288	104	
Fever; Post-Injection 1			
alternative assessment type: Systematic			
subjects affected / exposed[8]	86 / 1264 (6.80%)	42 / 635 (6.61%)	
occurrences (all)	86	42	
Fever; Post-Injection 2			
alternative assessment type: Systematic			
subjects affected / exposed[9]	72 / 1228 (5.86%)	42 / 594 (7.07%)	
occurrences (all)	72	42	
Fever; Post-Injection 3			
alternative assessment type: Systematic			
subjects affected / exposed[10]	89 / 1215 (7.33%)	52 / 597 (8.71%)	
occurrences (all)	89	52	
Malaise; Post-Injection 1			
alternative assessment type: Systematic			
subjects affected / exposed[11]	324 / 1323 (24.49%)	170 / 657 (25.88%)	
occurrences (all)	324	170	
Malaise; Post-Injection 2			
alternative assessment type: Systematic			
subjects affected / exposed[12]	270 / 1298 (20.80%)	106 / 639 (16.59%)	
occurrences (all)	270	106	

Malaise; Post-Injection 3 alternative assessment type: Systematic subjects affected / exposed[13] occurrences (all)	246 / 1277 (19.26%) 246	96 / 631 (15.21%) 96	
Myalgia; Post-Injection 2 alternative assessment type: Systematic subjects affected / exposed[14] occurrences (all)	273 / 1298 (21.03%) 273	101 / 639 (15.81%) 101	
Myalgia; Post-Injection 3 alternative assessment type: Systematic subjects affected / exposed[15] occurrences (all)	255 / 1277 (19.97%) 255	116 / 631 (18.38%) 116	
Asthenia; Post-Injection 1 alternative assessment type: Systematic subjects affected / exposed[16] occurrences (all)	326 / 1323 (24.64%) 326	148 / 657 (22.53%) 148	
Asthenia; Post-Injection 2 alternative assessment type: Systematic subjects affected / exposed[17] occurrences (all)	231 / 1298 (17.80%) 231	105 / 639 (16.43%) 105	
Asthenia; Post-Injection 3 alternative assessment type: Systematic subjects affected / exposed[18] occurrences (all)	208 / 1277 (16.29%) 208	110 / 631 (17.43%) 110	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed[19] occurrences (all)	55 / 1333 (4.13%) 60	33 / 664 (4.97%) 35	
Musculoskeletal and connective tissue disorders Myalgia; Post-Injection 1 alternative assessment type: Systematic subjects affected / exposed[20] occurrences (all)	386 / 1323 (29.18%) 386	180 / 657 (27.40%) 180	

Infections and infestations Nasopharyngitis subjects affected / exposed[21] occurrences (all)	150 / 1333 (11.25%) 163	60 / 664 (9.04%) 70	
Influenza subjects affected / exposed[22] occurrences (all)	76 / 1333 (5.70%) 80	37 / 664 (5.57%) 40	

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 an unsolicited adverse event recorded in a diary card within 28 days after any vaccination; 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 adverse event recorded in a diary card within 14 days after each vaccination; 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 adverse event recorded in a diary card within 14 days after each vaccination; 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 adverse event recorded in a diary card within 14 days after each vaccination; 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 adverse event recorded in a diary card within 7 days after each vaccination; 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 adverse event recorded in a diary card within 7 days after each vaccination; 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 adverse event recorded in a diary card within 7 days after each vaccination; 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[9] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[10] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[11] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[12] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[13] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[14] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[15] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[16] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[17] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[18] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[19] - 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 an unsolicited adverse event recorded in a diary card within 28 days after any vaccination; 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.

[20] - 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 adverse event recorded in a diary card within 14 days after each vaccination; 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.

[21] - 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 an unsolicited adverse event recorded in a diary card within 28 days after any vaccination; 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.

[22] - 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 an unsolicited adverse event recorded in a diary card within 28 days after any vaccination; 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
21 January 2011	Major modifications included Venezuela declined its participation, clarified efficacy during the Active Phase, end of febrile episode was further clarified, frequency of contact during the Hospital Phase was increased to 1 every 3 months, potential manifestations of severity were updated, clarified that the safety surveillance was conducted by the Principal Investigators, transaminases were available to add in the assessment of the severity of confirmed dengue cases, clarification on the reporting of SAEs during the Active Phase and the Hospital Phase, and clarification on subjects who discontinued from vaccination or trial and their continuation in the study for surveillance purposes.
03 August 2011	Clarified collection periods of acute and convalescent samples, SAE reporting period was extended throughout the entire study, clarified that laboratory staff was blinded to treatment allocation, age stratification was clarified (9 to 11 years and 12 to 16 years), updated time window of assessment of serious viscerotropic disease, and introduced the use of the World Health Organization Verbal Autopsy Questionnaire.
29 May 2013	Modified the testing algorithm for the virological-confirmation of dengue cases to maximize the likelihood of detecting dengue cases, updated and clarified text of secondary objectives as it relates to the assessment of the CYD dengue vaccine in preventing symptomatic virologically-confirmed cases, Hospital Phase was extended by 2 years to allow a 5 year follow-up period after the last vaccination, "Other Objectives" section was added, and included re-consenting of subjects for the 2-year extension and for additional testing to identify the dengue virus.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported