



Clinical trial results:

Immunogenicity and Safety of Tetravalent Dengue Vaccine Given in 1-, 2-, or 3-Dose Schedules (STAGE I) Followed by a Single Booster Injection of the Same Vaccine (STAGE II) 1 or 2 Years after the Last Primary Dose in Healthy Subjects 9 to 50 Years of Age in Colombia and the Philippines

Summary

EudraCT number	2020-002854-25
Trial protocol	Outside EU/EEA
Global end of trial date	29 April 2020

Results information

Result version number	v1 (current)
This version publication date	12 November 2020
First version publication date	12 November 2020

Trial information

Trial identification

Sponsor protocol code	CYD65
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02628444
WHO universal trial number (UTN)	U1111-1161-3242

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur
Sponsor organisation address	14, Espace Henry Vallée, Lyon, France, 69007
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 August 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

STAGE1:

- To demonstrate non-inferiority (NI) of immune response elicited against each dengue serotype by CYD dengue vaccine given as 2-dose schedule (Group 2) compared to immune response elicited by CYD dengue vaccine given as a 3-dose schedule (Group 1), in subjects seropositive at Baseline, 28 days post-final injection, and 1 year after last injection, both in terms of geometric mean ratio (GMR).

STAGE2:

- To demonstrate NI of immune response elicited against each dengue serotype by CYD dengue vaccine, in subjects seropositive at baseline, 28 days after administration of booster dose of CYD dengue vaccine, in terms of geometric mean of titer ratio (GMTR, within a group) or GMR (between groups):

Booster Dose at 1 Year

- Post-Year 1 booster Group 1/post-Dose-3 Group 1 (GMTR)
- Post-Year 1 booster Group 2/post-Dose 3 Group 1 (GMR)

Booster Dose at 2 Years

- Post-Year 2 booster Group 1/post-Dose 3 Group 1 (GMTR)
- Post-Year 2 booster Group 2/post-Dose 3 Group 1 (GMR)

Protection of trial subjects:

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: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Colombia: 525
Country: Number of subjects enrolled	Philippines: 525
Worldwide total number of subjects	1050
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)	162
Adolescents (12-17 years)	173
Adults (18-64 years)	715
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 6 active centers in 2 countries. A total of 1050 subjects were enrolled from 02 May 2016 to 16 September 2016.

Pre-assignment

Screening details:

Subjects were enrolled and randomised in 1:1:1 ratio to 1 of 3 treatment arms in STAGE-I. After STAGE-I, subjects identified as seropositive at Baseline were randomised in ratio 1:1 to 1 of 2 subgroups (a [1a,2a,3a] or b: [1b,2b,3b]) and received one CYD booster vaccine in STAGE-II at either 12 months (Subgroup a) or 24 months (Subgroup b).

Period 1

Period 1 title	STAGE-I (24 Months)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	STAGE-I Group 1: CYD Dengue Vaccine

Arm description:

Subjects received 3 doses of CYD dengue vaccine 0.5 millilitres (mL) subcutaneously (SC) at Day 0 (Vaccination 1), Month 6 (Vaccination 2), and Month 12 (Vaccination 3).

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

Dosage and administration details:

Subjects received 0.5 mL, SC injection at Day 0, Month 6, and Month 12, respectively, in the deltoid region of the upper arm.

Arm title	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)
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Arm description:

Subjects received a dose of placebo at Day 0 (Vaccination 1) along with 2 doses of CYD dengue vaccine 0.5 mL SC at Month 6 (Vaccination 2) and Month 12 (Vaccination 3).

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

Dosage and administration details:

Subject received 0.5 mL, SC injection at Month 6 and Month 12, respectively, in the deltoid region of the upper arm.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received 0.5 mL placebo matched to CYD vaccine, SC injection at Day 0 in the deltoid region of the upper arm.

Arm title	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)
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Arm description:

Subjects received 2 doses of placebo at Day 0 (Vaccination 1) and Month 6 (Vaccination 2) along with a dose of CYD dengue vaccine 0.5 mL SC at Month 12 (Vaccination 3).

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

Dosage and administration details:

Subject received 0.5 mL, SC injection at Month 12, in the deltoid region of the upper arm.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received 0.5 mL placebo matched to CYD vaccine, SC injection at Day 0 and Month 6, in the deltoid region of the upper arm.

Number of subjects in period 1	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)
Started	350	348	352
Vaccinated subjects	348	348	352
Full analysis set	333	328	332
Completed	314	309	310
Not completed	36	39	42
Adverse event (AE) intensity less than (<) Grade 1	1	-	-
Non-compliance with protocol	9	16	9
Lost to follow-up	5	3	5
Voluntary withdrawal not due to AE	21	16	25
Serious AE (SAE)	-	4	3

Period 2

Period 2 title	STAGE-II (18 Months)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
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Arm title	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)
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Arm description:

Subjects from Group 1 who received vaccination in STAGE-I; and were seropositive at Baseline received a booster dose of CYD dengue vaccine in STAGE-II at 1 year post last dose in STAGE-I (i.e., at Month 24).

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

Dosage and administration details:

Subject received 0.5 mL, booster SC injection after 1 year (or 12 months) post last dose in STAGE-I, in the deltoid region of the upper arm.

Arm title	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)
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Arm description:

Subjects from Group 2 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 1 year post last dose in STAGE-I (i.e., at Month 24).

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

Dosage and administration details:

Subject received 0.5 mL, booster SC injection after 1 year (or 12 months) post last dose in STAGE-I, in the deltoid region of the upper arm.

Arm title	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)
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Arm description:

Subjects from Group 3 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 1 year post last dose in STAGE-I (i.e., at Month 24).

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

Dosage and administration details:

Subject received 0.5 mL, booster SC injection after 1 year (or 12 months) post last dose in STAGE-I, in the deltoid region of the upper arm.

Arm title	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2
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	Years)
Arm description:	
Subjects from Group 1 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 2 years post last dose in STAGE-I (i.e., at Month 36).	
Arm type	Experimental
Investigational medicinal product name	CYD Dengue Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subject received 0.5 mL, booster SC injection after 2 years (or 24 months) post last dose in STAGE-I, in the deltoid region of the upper arm.

Arm title	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)
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Arm description:

Subjects from Group 2 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 2 years post last dose in STAGE-I (i.e., at Month 36).

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

Dosage and administration details:

Subject received 0.5 mL, booster SC injection after 2 years (or 24 months) post last dose in STAGE-I, in the deltoid region of the upper arm.

Arm title	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)
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Arm description:

Subjects from Group 3 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 2 years post last dose in STAGE-I (i.e., at Month 36).

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

Dosage and administration details:

Subject received 0.5 mL, booster SC injection after 2 years (or 24 months) post last dose in STAGE-I, in the deltoid region of the upper arm.

Number of subjects in period 2^[1]	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)
Started	145	152	157
Vaccinated	55	59	62
Completed	55	59	62
Not completed	90	93	95

SAE	-	3	-
Non-compliance with protocol	83	83	83
Lost to follow-up	1	1	2
Voluntary withdrawal not due to AE	5	6	10
Other AE	1	-	-

Number of subjects in period 2^[1]	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)
Started	149	152	151
Vaccinated	53	54	52
Completed	53	54	52
Not completed	96	98	99
SAE	-	2	3
Non-compliance with protocol	81	84	85
Lost to follow-up	3	1	2
Voluntary withdrawal not due to AE	12	11	9
Other AE	-	-	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Started indicates the number of subjects who had completed STAGE-I and were seropositive at Baseline.

Baseline characteristics

Reporting groups

Reporting group title	STAGE-I Group 1: CYD Dengue Vaccine
Reporting group description: Subjects received 3 doses of CYD dengue vaccine 0.5 millilitres (mL) subcutaneously (SC) at Day 0 (Vaccination 1), Month 6 (Vaccination 2), and Month 12 (Vaccination 3).	
Reporting group title	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)
Reporting group description: Subjects received a dose of placebo at Day 0 (Vaccination 1) along with 2 doses of CYD dengue vaccine 0.5 mL SC at Month 6 (Vaccination 2) and Month 12 (Vaccination 3).	
Reporting group title	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)
Reporting group description: Subjects received 2 doses of placebo at Day 0 (Vaccination 1) and Month 6 (Vaccination 2) along with a dose of CYD dengue vaccine 0.5 mL SC at Month 12 (Vaccination 3).	

Reporting group values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)
Number of subjects	350	348	352
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	30.8 ± 14.42	31.3 ± 14.47	31.1 ± 14.62
Gender categorical Units: Subjects			
Female	190	197	185
Male	160	151	167
Race Units: Subjects			
American Indian or Alaska Native	171	172	169
Asian	174	172	177
Black or African American	5	3	6
Native Hawaiian or Other Pacific Islander	0	0	0
White	0	1	0
Not Reported	0	0	0
Dengue Baseline Status			
Baseline dengue seropositive subjects were defined as subjects with greater than equal to (\geq) 10 (1/dilution [dil]) for at least 1 serotype with parental dengue virus strain. Baseline dengue seronegative subjects were defined as subjects with valid titer less than ($<$) 10 (1/dil) for all serotypes with parental dengue virus strains. Baseline dengue status was evaluated for subjects in full analysis set (FAS) that included subjects who had received either at least 1 injection of either CYD dengue vaccine or placebo and had at least 1 blood sample drawn and valid post-injection serology results.			
Units: Subjects			
Seropositive subjects	281	288	291
Seronegative subjects	52	40	41
Undetermined	17	20	20

Reporting group values	Total		
Number of subjects	1050		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	572		
Male	478		
Race Units: Subjects			
American Indian or Alaska Native	512		
Asian	523		
Black or African American	14		
Native Hawaiian or Other Pacific Islander	0		
White	1		
Not Reported	0		
Dengue Baseline Status			
Baseline dengue seropositive subjects were defined as subjects with greater than equal to (\geq) 10 (1/dilution [dil]) for at least 1 serotype with parental dengue virus strain. Baseline dengue seronegative subjects were defined as subjects with valid titer less than ($<$) 10 (1/dil) for all serotypes with parental dengue virus strains. Baseline dengue status was evaluated for subjects in full analysis set (FAS) that included subjects who had received either at least 1 injection of either CYD dengue vaccine or placebo and had at least 1 blood sample drawn and valid post-injection serology results.			
Units: Subjects			
Seropositive subjects	860		
Seronegative subjects	133		
Undetermined	57		

End points

End points reporting groups

Reporting group title	STAGE-I Group 1: CYD Dengue Vaccine
Reporting group description: Subjects received 3 doses of CYD dengue vaccine 0.5 millilitres (mL) subcutaneously (SC) at Day 0 (Vaccination 1), Month 6 (Vaccination 2), and Month 12 (Vaccination 3).	
Reporting group title	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)
Reporting group description: Subjects received a dose of placebo at Day 0 (Vaccination 1) along with 2 doses of CYD dengue vaccine 0.5 mL SC at Month 6 (Vaccination 2) and Month 12 (Vaccination 3).	
Reporting group title	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)
Reporting group description: Subjects received 2 doses of placebo at Day 0 (Vaccination 1) and Month 6 (Vaccination 2) along with a dose of CYD dengue vaccine 0.5 mL SC at Month 12 (Vaccination 3).	
Reporting group title	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)
Reporting group description: Subjects from Group 1 who received vaccination in STAGE-I; and were seropositive at Baseline received a booster dose of CYD dengue vaccine in STAGE-II at 1 year post last dose in STAGE-I (i.e., at Month 24).	
Reporting group title	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)
Reporting group description: Subjects from Group 2 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 1 year post last dose in STAGE-I (i.e., at Month 24).	
Reporting group title	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)
Reporting group description: Subjects from Group 3 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 1 year post last dose in STAGE-I (i.e., at Month 24).	
Reporting group title	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)
Reporting group description: Subjects from Group 1 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 2 years post last dose in STAGE-I (i.e., at Month 36).	
Reporting group title	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)
Reporting group description: Subjects from Group 2 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 2 years post last dose in STAGE-I (i.e., at Month 36).	
Reporting group title	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)
Reporting group description: Subjects from Group 3 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 2 years post last dose in STAGE-I (i.e., at Month 36).	
Subject analysis set title	Group 1: 28 days Post-dose 3 in STAGE-I
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects who received 3 doses of CYD dengue vaccine in STAGE-I, and were seropositive at Baseline were assessed 28 days after third CYD vaccine in STAGE-I.	
Subject analysis set title	Group 1a: 28 days post 12 month Booster dose
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from Group 1 (STAGE-I) who were seropositive at Baseline and received a booster dose at 1 year (or 12 months) post last dose in STAGE-I, were assessed 28 days after CYD dengue booster dose vaccination.

Subject analysis set title	Group 1b: 28 days post 24 month Booster dose
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from Group 1 (STAGE-I) who were seropositive at Baseline and received a booster dose at 2 years (or 24 months) post last dose in STAGE-I, were assessed 28 days after CYD dengue booster dose vaccination.

Subject analysis set title	Group 2a: 28 days post 12 month Booster dose
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from Group 2 (STAGE-I) who were seropositive at Baseline and received a booster dose at 1 year (or 12 months) post last dose in STAGE-I, were assessed 28 days after CYD dengue booster dose vaccination.

Subject analysis set title	Group 2b: 28 days post 24 month Booster dose
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from Group 2 (STAGE-I) who were seropositive at Baseline and received a booster dose at 2 years (or 24 months) post last dose in STAGE-I, were assessed 28 days after CYD dengue booster dose vaccination.

Primary: STAGE-I: Geometric Mean Titers (GMTs) Against Each Dengue Virus Serotype 28 Days After Last CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline

End point title	STAGE-I: Geometric Mean Titers (GMTs) Against Each Dengue Virus Serotype 28 Days After Last CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline ^[1]
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3, or 4) were assessed using plaque reduction neutralisation test (PRNT) assay method. Dengue seropositive subjects at Baseline: subjects with titers ≥ 10 (1/dil) for at least 1 serotype with parental dengue virus strains. Analysis performed on per-protocol analysis set (PPAS): all subjects who had no protocol violations; and who met any of following study violations were excluded from PPAS (STAGE I/II): had not met all protocol-specified inclusion/exclusion criteria, had not received correct doses or injections, received vaccine other than randomised schedule, did not receive the vaccination in proper time window, had not provided post-dose serology sample in proper time window, received protocol-restricted medication, therapy, or vaccine. Here, 'Number of subject analysed'=subjects with available data for this endpoint.

End point type	Primary
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End point timeframe:

28 days after last CYD dengue vaccination

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data for this endpoint was not planned to be collected and analysed for Group 3, as pre-specified in protocol.

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	265	272		
Units: titers				
geometric mean (confidence interval 95%)				
Serotype 1	822 (700 to 964)	899 (752 to 1075)		

Serotype 2	875 (770 to 995)	869 (754 to 1002)		
Serotype 3	610 (535 to 694)	599 (524 to 685)		
Serotype 4	531 (470 to 601)	510 (453 to 575)		

Statistical analyses

Statistical analysis title	Group 2/Group 1: Serotype 1
Statistical analysis description:	
The non-inferiority was demonstrated if the lower limit of the two-sided 95% confidence interval (CI) of the ratio of GMTs between groups (Group 2/Group 1) was greater than ($>$) 1/2. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.	
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	537
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.862
upper limit	1.39

Statistical analysis title	Group 2/Group 1: Serotype 2
Statistical analysis description:	
The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.	
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	537
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Ratio
Point estimate	0.993
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.2

Statistical analysis title	Group 2/Group 1: Serotype 3
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	537
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Ratio
Point estimate	0.983
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.816
upper limit	1.18

Statistical analysis title

Group 2/Group 1: Serotype 4

Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	537
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.809
upper limit	1.14

Primary: STAGE-I: Geometric Mean Titers Against Each Dengue Virus Serotype 1 Year After Last CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline

End point title	STAGE-I: Geometric Mean Titers Against Each Dengue Virus Serotype 1 Year After Last CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline ^[2]
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3 or 4) were assessed using the PRNT assay method. Titers were measured in terms of 1/dilution. Dengue seropositive subjects at Baseline were defined as subjects with titers ≥ 10 (1/dil) for at least one serotype with the parental dengue virus strains. Analysis was performed on PPAS. Here, 'Number of subject analysed' = subjects with available data for this endpoint.

End point type	Primary
End point timeframe:	
1 year after last CYD dengue vaccination	

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data for this endpoint was not planned to be collected and analysed for Group 3, as pre-specified in protocol.

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	190		
Units: titers				
geometric mean (confidence interval 95%)				
Serotype 1	490 (398 to 604)	504 (403 to 630)		
Serotype 2	821 (704 to 957)	737 (611 to 888)		
Serotype 3	477 (405 to 561)	437 (368 to 519)		
Serotype 4	270 (235 to 310)	238 (205 to 277)		

Statistical analyses

Statistical analysis title	Group 2/Group 1: Serotype 1
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	375
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.757
upper limit	1.4

Statistical analysis title	Group 2/Group 1: Serotype 2
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
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Number of subjects included in analysis	375
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	0.897
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.705
upper limit	1.14

Statistical analysis title	Group 2/Group 1: Serotype 3
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	375
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	0.917
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.724
upper limit	1.16

Statistical analysis title	Group 2/Group 1: Serotype 4
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	375
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	0.884
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.09

Primary: STAGE-II: Geometric Mean Titers Against Each Dengue Virus Serotype Within Group 1a and Group 1 After the Third Dose of CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline

End point title	STAGE-II: Geometric Mean Titers Against Each Dengue Virus Serotype Within Group 1a and Group 1 After the Third Dose of CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3 or 4) were assessed using the PRNT assay method. Titers were measured in terms of 1/dilution. Dengue seropositive subjects at Baseline were defined as subjects with titers ≥ 10 (1/dil) for at least one serotype with the parental dengue virus strains. Data of Group 1 (28 days after post-dose 3 in STAGE-I) and Group 1a (28 days post 12 month Booster dose) was reported and compared in this endpoint. GMT paired ratio (given in statistical analysis section) was calculated by dividing geometric mean values of Group 1a: 28 days post 12 months booster dose by Group 1: 28 days Post-dose 3 in STAGE-I. Analysis was performed on PPAS. Here, 'Number of subject analysed'=subjects with available data for this endpoint.

End point type	Primary
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End point timeframe:

Group 1: 28 days Post-dose 3 in STAGE-I, Group 1a: 28 days post 12 month booster dose

End point values	Group 1: 28 days Post-dose 3 in STAGE-I	Group 1a: 28 days post 12 month Booster dose		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	53	53		
Units: titers				
geometric mean (confidence interval 98.75%)				
Serotype 1	853 (526 to 1384)	483 (281 to 832)		
Serotype 2	1186 (809 to 1738)	884 (602 to 1300)		
Serotype 3	696 (483 to 1002)	722 (458 to 1140)		
Serotype 4	592 (400 to 876)	383 (269 to 545)		

Statistical analyses

Statistical analysis title	Group 1a Booster/Group 1 Post-dose 3: Serotype 1
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs within groups (Group 1a Booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	Group 1a: 28 days post 12 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
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Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT paired ratio
Point estimate	0.567
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.399
upper limit	0.805

Statistical analysis title	Group 1a Booster/Group 1 Post-dose 3: Serotype 2
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs within groups (Group 1a Booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	Group 1a: 28 days post 12 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT paired ratio
Point estimate	0.746
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.55
upper limit	1.01

Statistical analysis title	Group 1a Booster/Group 1 Post-dose 3: Serotype 3
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs within groups (Group 1a Booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	Group 1a: 28 days post 12 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT paired ratio
Point estimate	1.04
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.686
upper limit	1.57

Statistical analysis title	Group 1a Booster/Group 1 Post-dose 3: Serotype 4
Statistical analysis description: The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs within groups (Group 1a Booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.	
Comparison groups	Group 1a: 28 days post 12 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT paired ratio
Point estimate	0.647
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.434
upper limit	0.963

Primary: STAGE-II: Geometric Mean Titers Against Each Dengue Virus Serotype Comparison Between Group 2a and Group 1 After the Third Dose of CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline

End point title	STAGE-II: Geometric Mean Titers Against Each Dengue Virus Serotype Comparison Between Group 2a and Group 1 After the Third Dose of CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3 or 4) were assessed using the PRNT assay method. Titers were measured in terms of 1/dil. Dengue seropositive subjects at Baseline were defined as subjects with titers ≥ 10 (1/dil) for at least one serotype with the parental dengue virus strains. Data of Group 1 (28 days post-dose 3 in STAGE-I) and Group 2a (28 days post 12 months Booster dose) was reported and compared in this endpoint. GMT ratio (given in statistical analysis section) was calculated by dividing geometric mean values of Group 2a: 28 days post 12 months booster dose by Group 1: 28 days Post-dose 3 in STAGE-I. Analysis was performed on PPAS. Here, 'Number of subject analysed' = subjects with available data for this endpoint.

End point type	Primary
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End point timeframe:

Group 1: 28 days Post-dose 3 in STAGE-I, Group 2a: 28 days post 12 month booster dose

End point values	Group 1: 28 days Post-dose 3 in STAGE-I	Group 2a: 28 days post 12 month Booster dose		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	112	58		
Units: titers				
geometric mean (confidence interval 98.75%)				

Serotype 1	875 (614 to 1248)	549 (331 to 911)		
Serotype 2	1023 (771 to 1356)	828 (569 to 1203)		
Serotype 3	568 (433 to 745)	676 (436 to 1049)		
Serotype 4	540 (418 to 697)	270 (200 to 364)		

Statistical analyses

Statistical analysis title	Group 2a Booster/Group 1 Post-dose 3: Serotype 1
Statistical analysis description:	
The non-inferiority was demonstrated if the lower limit of the two-sided Bonferroni corrected 95% CI for the ratio of GMTs between groups (Group 2a Booster/Group 1) was $>1/2$. Overall non-inferiority was to be demonstrated if all 4 serotypes achieved non-inferiority.	
Comparison groups	Group 2a: 28 days post 12 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	0.627
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.342
upper limit	1.15

Statistical analysis title	Group 2a Booster/Group 1 Post-dose 3: Serotype 2
Statistical analysis description:	
The non-inferiority was demonstrated if the lower limit of the two-sided Bonferroni corrected 95% CI for the ratio of GMTs between groups (Group 2a Booster/Group 1) was $>1/2$. Overall non-inferiority was to be demonstrated if all 4 serotypes achieved non-inferiority.	
Comparison groups	Group 2a: 28 days post 12 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	0.809
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.505
upper limit	1.3

Statistical analysis title	Group 2a Booster/Group 1 Post-dose 3: Serotype 3
Statistical analysis description:	
The non-inferiority was demonstrated if the lower limit of the two-sided Bonferroni corrected 95% CI for the ratio of GMTs between groups (Group 2a Booster/Group 1) was $>1/2$. Overall non-inferiority was to be demonstrated if all 4 serotypes achieved non-inferiority.	
Comparison groups	Group 2a: 28 days post 12 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	1.19
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.732
upper limit	1.94

Statistical analysis title	Group 2a Booster/Group 1 Post-dose 3: Serotype 4
Statistical analysis description:	
The non-inferiority was demonstrated if the lower limit of the two-sided Bonferroni corrected 95% CI for the ratio of GMTs between groups (Group 2a Booster/Group 1) was $>1/2$. Overall non-inferiority was to be demonstrated if all 4 serotypes achieved non-inferiority.	
Comparison groups	Group 1: 28 days Post-dose 3 in STAGE-I v Group 2a: 28 days post 12 month Booster dose
Number of subjects included in analysis	170
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio
Point estimate	0.499
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.331
upper limit	0.754

Primary: STAGE-II: Geometric Mean Titers Against Each Dengue Virus Serotype Within Group 1b and Group 1 After the Third Dose of CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline

End point title	STAGE-II: Geometric Mean Titers Against Each Dengue Virus Serotype Within Group 1b and Group 1 After the Third Dose of CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3 or 4) were assessed using the PRNT assay method. Titers were measured in terms of 1/dil. Dengue seropositive subjects at Baseline were defined as subjects with titers ≥ 10 (1/dil) for at least one serotype with the parental dengue virus strains. Data of Group 1 (28 days Post-dose 3 in STAGE-I) and Group 1b (28 days post 24 month booster dose) was reported and compared in this endpoint. GMT paired ratio (given in statistical analysis section) was calculated by dividing geometric mean values of Group 1b: 28 days post 24 months booster dose by Group 1: 28 days Post-dose 3 in STAGE-I. Analysis was performed on PPAS. Here,

'Number of subject analysed'=subjects with available data for this endpoint.

End point type	Primary
End point timeframe:	
Group 1: 28 days Post-dose 3 in STAGE-I, Group 1b: 28 days post 24 month booster dose	

End point values	Group 1: 28 days Post-dose 3 in STAGE-I	Group 1b: 28 days post 24 month Booster dose		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	48		
Units: titers				
geometric mean (confidence interval 98.75%)				
Serotype 1	1017 (592 to 1746)	700 (401 to 1220)		
Serotype 2	838 (554 to 1269)	730 (497 to 1071)		
Serotype 3	486 (333 to 708)	559 (395 to 792)		
Serotype 4	556 (400 to 774)	364 (260 to 510)		

Statistical analyses

Statistical analysis title	Group 1b Booster/Group 1 Post-dose 3: Serotype 1
Statistical analysis description:	
The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs within groups (Group 1b booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.	
Comparison groups	Group 1b: 28 days post 24 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT paired ratio
Point estimate	0.688
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.479
upper limit	0.989

Statistical analysis title	Group 1b Booster/Group 1 Post-dose 3: Serotype 2
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs within groups (Group 1b booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	Group 1b: 28 days post 24 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT paired ratio
Point estimate	0.871
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.673
upper limit	1.13

Statistical analysis title	Group 1b Booster/Group 1 Post-dose 3: Serotype 3
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs within groups (Group 1b booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	Group 1b: 28 days post 24 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT paired ratio
Point estimate	1.15
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.887
upper limit	1.49

Statistical analysis title	Group 1b Booster/Group 1 Post-dose 3: Serotype 4
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs within groups (Group 1b booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	Group 1b: 28 days post 24 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT paired ratio
Point estimate	0.655
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.471
upper limit	0.911

Primary: STAGE-II: Geometric Mean Titers Against Each Dengue Virus Serotype Comparison Between Group 2b and Group 1 After the Third Dose of CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline

End point title	STAGE-II: Geometric Mean Titers Against Each Dengue Virus Serotype Comparison Between Group 2b and Group 1 After the Third Dose of CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3 or 4) were assessed using the PRNT assay method. Titers were measured in terms of 1/dilution. Dengue seropositive subjects at Baseline were defined as subjects with titers ≥ 10 (1/dil) for at least one serotype with the parental dengue virus strains. Data of Group 1 (28 days post-dose 3 in STAGE-I) and Group 2b (28 days post 12 months Booster dose) was reported and compared in this endpoint. GMT ratio (given in statistical analysis section) was calculated by dividing geometric mean values of Group 2b: 28 days post 24 months booster dose by Group 1: 28 days Post-dose 3 in STAGE-I. Analysis was performed on PPAS. Here, 'Number of subject analysed'=subjects with available data for this endpoint.

End point type	Primary
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End point timeframe:

Group 1: 28 days Post-dose 3 in STAGE-I, Group 2b: 28 days post 24 month Booster dose

End point values	Group 1: 28 days Post-dose 3 in STAGE-I	Group 2b: 28 days post 24 month Booster dose		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	112	50		
Units: titers				
geometric mean (confidence interval 98.75%)				
Serotype 1	875 (614 to 1248)	778 (429 to 1414)		
Serotype 2	1023 (771 to 1356)	692 (430 to 1116)		
Serotype 3	568 (433 to 745)	517 (365 to 733)		
Serotype 4	540 (418 to 697)	379 (261 to 551)		

Statistical analyses

Statistical analysis title	Group 2b Booster/Group 1 Post-dose 3: Serotype 1
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2b booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	Group 2b: 28 days post 24 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
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Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT ratio
Point estimate	0.889
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.462
upper limit	1.71

Statistical analysis title	Group 2b Booster/Group 1 Post-dose 3: Serotype 2
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2b booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	Group 2b: 28 days post 24 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT ratio
Point estimate	0.677
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.402
upper limit	1.14

Statistical analysis title	Group 2b Booster/Group 1 Post-dose 3: Serotype 3
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Statistical analysis description:

The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2b booster/Group 1) was $>1/2$. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.

Comparison groups	Group 2b: 28 days post 24 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT ratio
Point estimate	0.911
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.573
upper limit	1.45

Statistical analysis title	Group 2b Booster/Group 1 Post-dose 3: Serotype 4
Statistical analysis description: The non-inferiority was demonstrated if the lower limit of the two-sided 95% CI of the ratio of GMTs between groups (Group 2b booster/Group 1) was >1/2. Overall non-inferiority was demonstrated if all 4 serotypes achieved non-inferiority.	
Comparison groups	Group 2b: 28 days post 24 month Booster dose v Group 1: 28 days Post-dose 3 in STAGE-I
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT ratio
Point estimate	0.702
Confidence interval	
level	Other: 98.75 %
sides	2-sided
lower limit	0.447
upper limit	1.1

Secondary: STAGE-I: Geometric Mean Titers Against Each Serotype With the Parental Dengue Virus Strains After CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline

End point title	STAGE-I: Geometric Mean Titers Against Each Serotype With the Parental Dengue Virus Strains After CYD Dengue Vaccination in Subjects Who Were Seropositive at Baseline ^[3]
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3 or 4) were assessed using the PRNT assay method. Titers were measured in terms of 1/dilution. Dengue seropositive subjects at Baseline were defined as subjects with titers ≥ 10 (1/dil) for at least one serotype with the parental dengue virus strains. Analysis was performed on FAS that included the subjects who had received either at least one injection of CYD dengue vaccine or placebo; and had at least one blood sample drawn and valid post-injection serology results. Here, 'Number of subject analysed'=subjects with available data for this endpoint and 'n' = subjects with available data for each specified category. Here, 'vacc.' in categories indicates 'vaccination'.

End point type	Secondary
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End point timeframe:

28 days and 1 year after last CYD dengue vaccination

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data were collected and analysed for the applicable arms only.

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	281	288		
Units: titers				
geometric mean (confidence interval 95%)				

28 days after last vacc.:Serotype 1 (n=274,282)	834 (713 to 975)	877 (737 to 1043)		
28 days after last vacc.:Serotype 2 (n=274, 282)	879 (775 to 997)	870 (758 to 1000)		
28 days after last vacc.:Serotype 3 (n=274, 282)	620 (545 to 704)	602 (529 to 686)		
28 days after last vacc.:Serotype 4 (n=274, 282)	527 (467 to 595)	507 (451 to 570)		
1 year after last vacc.:Serotype 1 (n=192, 197)	498 (406 to 611)	512 (411 to 638)		
1 year after last vacc.:Serotype 2 (n=192, 197)	815 (702 to 947)	747 (622 to 897)		
1 year after last vacc.:Serotype 3 (n=192, 197)	477 (407 to 558)	444 (376 to 525)		
1 year after last vacc.:Serotype 4 (n=192, 197)	263 (230 to 302)	241 (208 to 279)		

Statistical analyses

Statistical analysis title	Group2/Group1: Serotype 1(28days after last vacc.)
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	569
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT Ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.833
upper limit	1.33

Statistical analysis title	Group2/Group1: Serotype2 (28days after last vacc.)
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	569
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT Ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.821
upper limit	1.19

Statistical analysis title	Group2/Group1: Serotype3 (28days after last vacc.)
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	569
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT Ratio
Point estimate	0.972
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.17

Statistical analysis title	Group2/Group1: Serotype4 (28days after last vacc.)
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	569
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT Ratio
Point estimate	0.963
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.814
upper limit	1.14

Statistical analysis title	Group2/Group1: Serotype1 (1 year after last vacc.)
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	569
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.762
upper limit	1.39

Statistical analysis title	Group2/Group1: Serotype2 (1 year after last vacc.)
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine

Number of subjects included in analysis	569
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT Ratio
Point estimate	0.917
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.724
upper limit	1.16

Statistical analysis title	Group2/Group1: Serotype3 (1 year after last vacc.)
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	569
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT Ratio
Point estimate	0.933
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.742
upper limit	1.17

Statistical analysis title	Group2/Group1: Serotype4 (1 year after last vacc.)
Comparison groups	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12) v STAGE-I Group 1: CYD Dengue Vaccine
Number of subjects included in analysis	569
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMT Ratio
Point estimate	0.916
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.12

Secondary: STAGE-I: Geometric Mean Titers Against Each Serotype With the Parental Dengue Virus Strains in All Subjects

End point title	STAGE-I: Geometric Mean Titers Against Each Serotype With the Parental Dengue Virus Strains in All Subjects
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (parental strains) were assessed using

the PRNT assay method. Analysis was performed on FAS. Here, 'n' = subjects with available data for each specified category. Here, 'vacc.' in categories indicates 'vaccination'.

End point type	Secondary
End point timeframe:	
Baseline, 28 days post vaccination 3, and 1 year post vaccination 3	

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	333	328	332	
Units: titers				
geometric mean (confidence interval 95%)				
Serotype 1: Baseline (n=333,328,332)	131 (103 to 165)	187 (147 to 237)	198 (157 to 250)	
Serotype 1: 28 days post vacc. 3 (n=326,322,324)	497 (410 to 602)	586 (482 to 714)	735 (589 to 916)	
Serotype 1: 1 year post vacc. 3 (n=231,232,230)	259 (200 to 336)	279 (213 to 365)	331 (252 to 435)	
Serotype 2: Baseline (n=333,328,332)	172 (138 to 214)	202 (163 to 252)	181 (147 to 222)	
Serotype 2: 28 days post vacc.3 (n=326,322,324)	567 (482 to 666)	628 (532 to 741)	734 (614 to 878)	
Serotype 2: 1 year post vacc. 3 (n=231,232,230)	470 (380 to 582)	457 (364 to 574)	500 (402 to 623)	
Serotype 3: Baseline (n=333,328,332)	163 (131 to 202)	180 (145 to 222)	169 (138 to 207)	
Serotype 3: 28 days post vacc.3 (n=326,322,324)	432 (373 to 500)	446 (383 to 519)	505 (428 to 595)	
Serotype 3: 1 year post vacc. 3 (n=231,232,230)	294 (240 to 361)	288 (235 to 354)	258 (213 to 312)	
Serotype 4: Baseline (n=333,328,332)	86.7 (71.4 to 105)	83.8 (69.9 to 100)	81.2 (67.7 to 97.4)	
Serotype 4: 28 days post vacc.3 (n=326,322,324)	429 (380 to 484)	441 (392 to 496)	546 (475 to 629)	
Serotype 4: 1 year post vacc. 3 (n=231,232,230)	203 (176 to 235)	192 (164 to 226)	177 (150 to 210)	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-I: Geometric Mean Titers Against Each Serotype With the Parental Dengue Virus Strains (by Baseline Dengue Status) in Subjects Who Were Seropositive and Seronegative at Baseline

End point title	STAGE-I: Geometric Mean Titers Against Each Serotype With the Parental Dengue Virus Strains (by Baseline Dengue Status) in Subjects Who Were Seropositive and Seronegative at Baseline
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3, or 4) were assessed using the PRNT assay. Dengue seropositive subjects at Baseline were defined as subjects with titers ≥ 10 (1/dil) for at least one serotype with the parental dengue virus strains. Dengue seronegative subjects at Baseline were defined as the subjects with valid titer < 10 (1/dil) for all serotypes with parental dengue virus strains. Titers were measured in terms of 1/dil. Analysis was performed on FAS. Here, 'number of subjects analysed'=subjects evaluable for this endpoint and 'n'=subjects with available data for each specified category. Here, 'vacc.' in categories indicates 'vaccination'; 'SP' and 'SN' in categories indicates 'seropositive' and 'seronegative', respectively; '99999' is used as space filler and specify that the 95% CI was not computable as the standard deviation of the sample was 0, since all subjects had the same value.

End point type	Secondary
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End point timeframe:

Baseline, 28 days post vaccination 3, and 1 year post vaccination 3

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	281	288	291	
Units: titers				
geometric mean (confidence interval 95%)				
SP- Serotype1: Baseline (n=281,288,291)	239 (194 to 295)	304 (244 to 379)	328 (267 to 404)	
SP- Serotype1: 28 days post inj. 3 (n=274,282,285)	834 (713 to 975)	877 (737 to 1043)	1201 (1007 to 1431)	
SP- Serotype1: 1 year post inj. 3 (n=192,197,197)	498 (406 to 611)	512 (411 to 638)	618 (500 to 764)	
SP- Serotype2: Baseline (n=281,288,291)	331 (279 to 394)	326 (271 to 393)	293 (247 to 347)	
SP- Serotype2: 28 days post inj. 3 (n=274,282,285)	879 (775 to 997)	870 (758 to 1000)	1046 (912 to 1201)	
SP- Serotype2: 1 year post inj. 3 (n=192,197,197)	815 (702 to 947)	747 (622 to 897)	798 (676 to 942)	
SP- Serotype3: Baseline (n=281,288,291)	310 (263 to 367)	290 (241 to 349)	269 (227 to 319)	
SP- Serotype3: 28 days post inj. 3 (n=274,282,285)	620 (545 to 704)	602 (529 to 686)	694 (604 to 797)	
SP- Serotype3: 1 year post inj. 3 (n=192,197,197)	477 (407 to 558)	444 (376 to 525)	390 (338 to 450)	
SP- Serotype4: Baseline (n=281,288,291)	147 (124 to 174)	123 (104 to 144)	118 (100 to 140)	
SP- Serotype4: 28 days post inj. 3 (n=274,282,285)	527 (467 to 595)	507 (451 to 570)	581 (507 to 666)	
SP- Serotype4: 1 year post inj. 3 (n=192,197,197)	263 (230 to 302)	241 (208 to 279)	227 (194 to 265)	
SN- Serotype1: Baseline (n=52,40,41)	5.00 (-99999 to 99999)	5.57 (4.65 to 6.67)	5.49 (4.75 to 6.34)	
SN- Serotype1: 28 days post inj. 3 (n=52,40,39)	32.4 (23.1 to 45.6)	34.3 (23.8 to 49.4)	20.2 (12.0 to 34.1)	
SN- Serotype1: 1 year post inj. 3 (n=39,35,33)	10.4 (7.12 to 15.1)	9.01 (6.30 to 12.9)	8.04 (5.86 to 11.0)	
SN- Serotype2: Baseline (n=52,40,41)	5.00 (-99999 to 99999)	6.47 (4.43 to 9.45)	5.86 (4.99 to 6.89)	

SN- Serotype2: 28 days post inj. 3 (n=52,40,39)	56.2 (40.1 to 78.7)	63.0 (37.5 to 106)	55.2 (27.8 to 110)	
SN- Serotype2: 1 year post inj. 3 (n=39,35,33)	31.3 (20.2 to 48.6)	28.7 (17.3 to 47.7)	30.9 (17.5 to 54.5)	
SN- Serotype3: Baseline (n=52,40,41)	5.00 (-99999 to 99999)	5.69 (4.86 to 6.66)	6.09 (5.05 to 7.34)	
SN- Serotype3: 28 days post inj. 3 (n=52,40,39)	64.2 (48.6 to 84.9)	53.7 (36.1 to 80.0)	49.5 (30.1 to 81.5)	
SN- Serotype3: 1 year post inj. 3 (n=39,35,33)	27.5 (17.4 to 43.5)	25.3 (15.8 to 40.3)	21.8 (13.6 to 35.0)	
SN- Serotype4: Baseline (n=52,40,41)	5.00 (-99999 to 99999)	5.41 (4.61 to 6.35)	5.64 (4.90 to 6.50)	
SN- Serotype4: 28 days post inj. 3 (n=52,40,39)	145 (112 to 187)	164 (114 to 237)	349 (189 to 646)	
SN- Serotype4: 1 year post inj. 3 (n=39,35,33)	57.1 (42.5 to 76.8)	53.8 (32.0 to 90.5)	40.8 (24.9 to 66.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-I: Percentage of Subjects With Antibodies Titer ≥ 10 (1/Dilution) Against Each Serotype With the Parental Dengue Virus Strains in All Subjects

End point title	STAGE-I: Percentage of Subjects With Antibodies Titer ≥ 10 (1/Dilution) Against Each Serotype With the Parental Dengue Virus Strains in All Subjects
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3 or 4) were assessed using the PRNT assay. Analysis was performed on FAS. Here, 'n' = subjects with available data for each specified category. Here, 'vacc.' in categories indicates 'vaccination'.

End point type	Secondary
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End point timeframe:

Baseline, 28 days post vaccination 3, and 1 year post vaccination 3

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	333	328	332	
Units: percentage of subjects				
number (confidence interval 95%)				
Serotype 1: Baseline (n=333,328,332)	77.8 (72.9 to 82.1)	80.5 (75.8 to 84.6)	83.4 (79.0 to 87.3)	
Serotype 1: 28 days post vacc.3 (n=326,322,324)	96.3 (93.7 to 98.1)	97.2 (94.8 to 98.7)	94.1 (91.0 to 96.4)	
Serotype 1: 1 year post vacc.3 (n=231,232,230)	88.3 (83.5 to 92.2)	87.5 (82.5 to 91.5)	88.3 (83.4 to 92.1)	
Serotype 2: Baseline (n=333,328,332)	82.6 (78.1 to 86.5)	83.8 (79.4 to 87.7)	85.2 (81.0 to 88.9)	

Serotype 2: 28 days post vacc.3 (n=326,322,324)	98.2 (96.0 to 99.3)	96.6 (94.0 to 98.3)	96.0 (93.2 to 97.8)	
Serotype 2: 1 year post vacc.3 (n=231,232,230)	95.7 (92.2 to 97.9)	94.4 (90.6 to 97.0)	94.8 (91.1 to 97.3)	
Serotype 3: Baseline (n=333,328,332)	82.6 (78.1 to 86.5)	84.1 (79.7 to 87.9)	87.0 (83.0 to 90.5)	
Serotype 3: 28 days post vacc.3 (n=326,322,324)	98.5 (96.5 to 99.5)	98.1 (96.0 to 99.3)	97.5 (95.2 to 98.9)	
Serotype 3: 1 year post vacc.3 (n=231,232,230)	95.7 (92.2 to 97.9)	95.7 (92.2 to 97.9)	94.3 (90.5 to 97.0)	
Serotype 4: Baseline (n=333,328,332)	79.6 (74.8 to 83.8)	81.4 (76.8 to 85.5)	81.6 (77.0 to 85.6)	
Serotype 4: 28 days post vacc.3 (n=326,322,324)	99.7 (98.3 to 100.0)	99.4 (97.8 to 99.9)	98.8 (96.9 to 99.7)	
Serotype 4: 1 year post vacc.3 (n=231,232,230)	99.1 (96.9 to 99.9)	96.6 (93.3 to 98.5)	95.7 (92.1 to 97.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-II: Percentage of Subjects With Antibodies Titer ≥ 10 (1/Dilution) Against Each Serotype With the Parental Dengue Virus Strain in Subjects Seropositive at Baseline

End point title	STAGE-II: Percentage of Subjects With Antibodies Titer ≥ 10 (1/Dilution) Against Each Serotype With the Parental Dengue Virus Strain in Subjects Seropositive at Baseline
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotypes (1, 2, 3 or 4) were assessed using the PRNT assay. Dengue seropositive subjects at Baseline were defined as subjects with titers ≥ 10 (1/dil) for at least one serotype with the parental dengue virus strains. Analysis was performed on FAS. Here, 'Number of subject analysed'=subjects with available data for this endpoint and 'n' = subjects with available data for each specified category. Here, 'vacc.' in categories indicates 'vaccination'; 28d indicates 28 days and 1yr indicates 1 year.

End point type	Secondary
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End point timeframe:

Baseline, 28 days post vaccination 3, and 1 year post vaccination 3

End point values	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	141	144	147	140
Units: percentage of subjects				
number (confidence interval 95%)				
Serotype1: Baseline (n=141,144,147,140,144,144)	92.2 (86.5 to 96.0)	90.3 (84.2 to 94.6)	91.8 (86.2 to 95.7)	92.1 (86.4 to 96.0)
Serotype1:28dpostvacc.3(n=137,140,145,137,142,140)	100.0 (97.3 to 100.0)	99.3 (96.1 to 100.0)	100.0 (97.5 to 100.0)	99.3 (96.0 to 100.0)
Serotype1:1yrpostvacc.3(n=137,138,143,128,130,131)	100.0 (97.3 to 100.0)	99.3 (96.0 to 100.0)	99.3 (96.2 to 100.0)	100.0 (97.2 to 100.0)

Serotype2: Baseline(n=141,144,147,140,144,144)	99.3 (96.1 to 100.0)	94.4 (89.3 to 97.6)	94.6 (89.6 to 97.6)	96.4 (91.9 to 98.8)
Serotype2:28dpostvacc.3(n=137,140,145,137,142,140)	100.0 (97.3 to 100.0)	99.3 (96.1 to 100.0)	100.0 (97.5 to 100.0)	100.0 (97.3 to 100.0)
Serotype2:1yrpostvacc.3(n=137,138,143,128,130,131)	100.0 (97.3 to 100.0)	99.3 (96.0 to 100.0)	100.0 (97.5 to 100.0)	100.0 (97.2 to 100.0)
Serotype3: Baseline(n=141,144,147,140,144,144)	98.6 (95.0 to 99.8)	96.5 (92.1 to 98.9)	95.2 (90.4 to 98.1)	97.1 (92.8 to 99.2)
Serotype3:28dpostvacc.3(n=137,140,145,137,142,140)	100.0 (97.3 to 100.0)	100.0 (97.4 to 100.0)	100.0 (97.5 to 100.0)	99.3 (96.0 to 100.0)
Serotype3:1yrpostvacc.3(n=137,138,143,128,130,131)	100.0 (97.3 to 100.0)	99.3 (96.0 to 100.0)	99.3 (96.2 to 100.0)	100.0 (97.2 to 100.0)
Serotype4: Baseline(n=141,144,147,140,144,144)	93.6 (88.2 to 97.0)	93.1 (87.6 to 96.6)	89.8 (83.7 to 94.2)	95.0 (90.0 to 98.0)
Serotype4:28dpostvacc.3(n=137,140,145,137,142,140)	100.0 (97.3 to 100.0)	100.0 (97.4 to 100.0)	100.0 (97.5 to 100.0)	100.0 (97.3 to 100.0)
Serotype4:1yrpostvacc.3(n=137,138,143,128,130,131)	100.0 (97.3 to 100.0)	99.3 (96.0 to 100.0)	98.6 (95.0 to 99.8)	100.0 (97.2 to 100.0)

End point values	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	144		
Units: percentage of subjects				
number (confidence interval 95%)				
Serotype1: Baseline (n=141,144,147,140,144,144)	91.7 (85.9 to 95.6)	97.2 (93.0 to 99.2)		
Serotype1:28dpostvacc.3(n=137,140,145,137,142,140)	99.3 (96.1 to 100.0)	100.0 (97.4 to 100.0)		
Serotype1:1yrpostvacc.3(n=137,138,143,128,130,131)	96.9 (92.3 to 99.2)	98.5 (94.6 to 99.8)		
Serotype2: Baseline(n=141,144,147,140,144,144)	94.4 (89.3 to 97.6)	97.2 (93.0 to 99.2)		
Serotype2:28dpostvacc.3(n=137,140,145,137,142,140)	99.3 (96.1 to 100.0)	100.0 (97.4 to 100.0)		
Serotype2:1yrpostvacc.3(n=137,138,143,128,130,131)	98.5 (94.6 to 99.8)	100.0 (97.2 to 100.0)		
Serotype3: Baseline(n=141,144,147,140,144,144)	93.1 (87.6 to 96.6)	100.0 (97.5 to 100.0)		
Serotype3:28dpostvacc.3(n=137,140,145,137,142,140)	100.0 (97.4 to 100.0)	100.0 (97.4 to 100.0)		
Serotype3:1yrpostvacc.3(n=137,138,143,128,130,131)	100.0 (97.2 to 100.0)	100.0 (97.2 to 100.0)		
Serotype4: Baseline(n=141,144,147,140,144,144)	91.7 (85.9 to 95.6)	94.4 (89.3 to 97.6)		
Serotype4:28dpostvacc.3(n=137,140,145,137,142,140)	100.0 (97.4 to 100.0)	100.0 (97.4 to 100.0)		
Serotype4:1yrpostvacc.3(n=137,138,143,128,130,131)	98.5 (94.6 to 99.8)	100.0 (97.2 to 100.0)		

Statistical analyses

Secondary: STAGE-II: Geometric Mean Titers Against Each Serotype With the Parental Dengue Virus Strains After Booster CYD Dengue Vaccination in Subjects Seropositive at Baseline

End point title	STAGE-II: Geometric Mean Titers Against Each Serotype With the Parental Dengue Virus Strains After Booster CYD Dengue Vaccination in Subjects Seropositive at Baseline
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End point description:

GMTs of antibodies against each of the 4 dengue virus serotype (1, 2, 3, or 4) were assessed using the PRNT assay. Dengue seropositive subjects at Baseline were defined as subjects with titers ≥ 10 (1/dil) for at least one serotype with the parental dengue virus strains. Titers were measured in terms of 1/dilution. Analysis was performed on FAS. Here, 'Number of subject analysed' = subjects with available data for this endpoint and 'n' = subjects with available data for each specified category. Here, 'vacc.' in categories indicates 'vaccination'.

End point type	Secondary
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End point timeframe:

Baseline, 28 days post vaccination-3, and 28 days post booster dose

End point values	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	141	144	147	140
Units: titers				
geometric mean (confidence interval 95%)				
Serotype1: Baseline (n=141,144,147,140,144,144)	246 (183 to 331)	283 (207 to 385)	309 (227 to 421)	231 (171 to 313)
Serotype1:28daypostvacc3(n=137,140,145,137,142,140)	828 (671 to 1022)	933 (730 to 1192)	1111 (868 to 1423)	840 (664 to 1061)
Serotype1:28daypostboosterdose(n=55,59,62,53,54,52)	505 (335 to 763)	552 (375 to 812)	861 (572 to 1297)	707 (472 to 1057)
Serotype2:Baseline(n=141,144,147,140,144,144)	370 (295 to 466)	335 (258 to 437)	283 (221 to 363)	296 (228 to 385)
Serotype2:28daypostvacc3(n=137,140,145,137,142,140)	986 (834 to 1166)	897 (735 to 1096)	1018 (850 to 1218)	783 (648 to 947)
Serotype2:28daypostboosterdose(n=55,59,62,53,54,52)	856 (638 to 1147)	858 (639 to 1152)	867 (640 to 1174)	813 (600 to 1100)
Serotype3:Baseline(n=141,144,147,140,144,144)	363 (285 to 462)	399 (308 to 519)	287 (222 to 371)	266 (211 to 335)
Serotype3:28daypostvacc3(n=137,140,145,137,142,140)	733 (617 to 871)	659 (547 to 794)	725 (607 to 865)	524 (434 to 631)
Serotype3:28daypostboosterdose(n=55,59,62,53,54,52)	721 (511 to 1018)	667 (477 to 933)	743 (557 to 992)	586 (455 to 754)
Serotype4:Baseline(n=141,144,147,140,144,144)	147 (114 to 190)	142 (113 to 178)	115 (89.6 to 146)	147 (117 to 183)
Serotype4:28daypostvacc3(n=137,140,145,137,142,140)	512 (433 to 605)	536 (456 to 631)	570 (463 to 701)	543 (456 to 647)
Serotype4:28daypostboosterdose(n=55,59,62,53,54,52)	380 (292 to 495)	265 (210 to 334)	300 (223 to 405)	368 (290 to 466)

End point values	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	144	144		
Units: titers				
geometric mean (confidence interval 95%)				
Serotype1: Baseline (n=141,144,147,140,144,144)	327 (239 to 447)	350 (265 to 462)		
Serotype1:28daypostvacc3(n=137,140,145,137,142,140)	824 (644 to 1056)	1301 (1011 to 1675)		
Serotype1:28daypostboosterdose(n=55,59,62,53,54,52)	749 (465 to 1207)	1199 (755 to 1902)		
Serotype2:Baseline(n=141,144,147,140,144,144)	318 (244 to 413)	303 (241 to 382)		
Serotype2:28daypostvacc3(n=137,140,145,137,142,140)	844 (695 to 1025)	1077 (871 to 1331)		
Serotype2:28daypostboosterdose(n=55,59,62,53,54,52)	655 (461 to 931)	967 (697 to 1343)		
Serotype3:Baseline(n=141,144,147,140,144,144)	210 (164 to 271)	253 (201 to 317)		
Serotype3:28daypostvacc3(n=137,140,145,137,142,140)	551 (459 to 661)	663 (534 to 823)		
Serotype3:28daypostboosterdose(n=55,59,62,53,54,52)	477 (364 to 626)	506 (370 to 691)		
Serotype4:Baseline(n=141,144,147,140,144,144)	106 (84.5 to 133)	122 (97.3 to 153)		
Serotype4:28daypostvacc3(n=137,140,145,137,142,140)	480 (406 to 568)	593 (495 to 711)		
Serotype4:28daypostboosterdose(n=55,59,62,53,54,52)	360 (273 to 474)	413 (297 to 574)		

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-I: Number of Subjects With Immediate Unsolicited Adverse Events Following Vaccination With CYD Dengue Vaccine or Placebo (Post Any Vaccination)

End point title	STAGE-I: Number of Subjects With Immediate Unsolicited Adverse Events Following Vaccination With CYD Dengue Vaccine or Placebo (Post Any Vaccination)
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End point description:

An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An unsolicited AE was an observed AE that does not fulfill the conditions prelisted in the electronic case report form (eCRF) in terms of diagnosis and/or onset post-vaccination. Immediate unsolicited AE were AEs that occurred within 30 minutes after any vaccination. Analysis was performed on safety analysis set (SafAS) that included subjects who had received at least one injection of either CYD dengue vaccine or placebo.

End point type	Secondary
End point timeframe:	
Within 30 minutes after any vaccination (1, 2, or 3)	

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	348	348	352	
Units: subjects	0	3	0	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-II: Number of Subjects With Immediate Unsolicited Adverse Events Following Booster Vaccination With CYD Dengue Vaccine

End point title	STAGE-II: Number of Subjects With Immediate Unsolicited Adverse Events Following Booster Vaccination With CYD Dengue Vaccine
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End point description:

An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An unsolicited AE was an observed AE that does not fulfill the conditions prelisted in the eCRF in terms of diagnosis and / or onset post-vaccination. Immediate unsolicited AE were AEs that occurred within 30 minutes after vaccination. Analysis was performed on SafAS.

End point type	Secondary
End point timeframe:	
Within 30 minutes after CYD booster vaccination	

End point values	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	59	62	53
Units: subjects	0	0	0	0

End point values	STAGE-II Group 2b: Placebo + CYD	STAGE-II Group 3b: Placebo + CYD		
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	+ CYD Booster (2 Years)	+ CYD Booster (2 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	53		
Units: subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-I: Number of Subjects With Solicited Injection Site Reactions Following Vaccination With CYD Dengue Vaccine or Placebo (Post Any Vaccination)

End point title	STAGE-I: Number of Subjects With Solicited Injection Site Reactions Following Vaccination With CYD Dengue Vaccine or Placebo (Post Any Vaccination)
End point description:	
Adverse reaction (AR) was defined as all noxious and unintended responses to a medicinal product related to any dose. A Solicited Reaction (SR) was defined as an AR observed and reported under the conditions (symptom and onset) prelisted (i.e., solicited) in the eCRF and considered as related to vaccination. Solicited injection site reaction was an AR at and around the injection site that included pain, erythema, and swelling. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category.	
End point type	Secondary
End point timeframe:	
Within 7 days after any vaccination (1, 2, or 3)	

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	348	348	352	
Units: subjects				
Pain (n=347,347,352)	109	114	97	
Erythema (n=347,347,352)	4	3	3	
Swelling (n=347,347,352)	2	5	5	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-I: Number of Subjects With Solicited Injection Site Reactions Following Vaccination With CYD Dengue Vaccine or Placebo (Post Each Vaccination)

End point title	STAGE-I: Number of Subjects With Solicited Injection Site Reactions Following Vaccination With CYD Dengue Vaccine or Placebo (Post Each Vaccination)
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End point description:

AR was defined as all noxious and unintended responses to a medicinal product related to any dose. An SR was defined as an AR observed and reported under the conditions (symptom and onset) prelisted (i.e., solicited) in the eCRF and considered as related to vaccination. Solicited injection site reaction was an AR at and around the injection site that included pain, erythema, and swelling. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary
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End point timeframe:

Within 7 days after each vaccination (1, 2, and 3)

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	348	348	352	
Units: subjects				
Post-vacc. 1: Pain (n=347,347,352)	61	61	61	
Post-vacc. 1: Erythema (n=347,347,352)	3	3	2	
Post vacc. 1: Swelling (n=347,347,352)	0	2	2	
Post-vacc. 2: Pain (n=332,328,332)	50	53	50	
Post-vacc. 2: Erythema (n=332,328,332)	1	0	1	
Post-vacc. 2: Swelling (n=332,328,332)	1	1	2	
Post-vacc. 3: Pain (n=325,321,324)	43	49	35	
Post-vacc. 3: Erythema (n=325,321,324)	0	0	1	
Post-vacc. 3: Swelling (n=325,321,324)	1	2	2	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-I: Number of Subjects With Solicited Systemic Reactions Following Vaccination With CYD Dengue Vaccine or Placebo (Post Any Vaccination)

End point title	STAGE-I: Number of Subjects With Solicited Systemic Reactions Following Vaccination With CYD Dengue Vaccine or Placebo (Post Any Vaccination)
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End point description:

An AR was defined as all noxious and unintended responses to a medicinal product related to any dose. An SR was defined as an AR observed and reported under the conditions (symptom and onset) prelisted (i.e., solicited) in the eCRF and considered as related to vaccination. Systemic AEs were all AEs that were not injection site reactions. Solicited systemic reactions included fever, headache, malaise, myalgia, and asthenia. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary
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End point timeframe:

Within 14 days after any vaccination (1, 2, or 3)

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	348	348	352	
Units: subjects				
Fever (n=347,347,352)	29	21	31	
Headache (n=347,347,352)	129	122	124	
Malaise (n=347,347,352)	114	98	102	
Myalgia (n=347,347,352)	110	92	86	
Asthenia (n=347,347,352)	98	80	71	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-I: Number of Subjects With Solicited Systemic Reactions Following Vaccination With CYD Dengue Vaccine or Placebo (Post Each Vaccination)

End point title	STAGE-I: Number of Subjects With Solicited Systemic Reactions Following Vaccination With CYD Dengue Vaccine or Placebo (Post Each Vaccination)
End point description:	An AR was defined as all noxious and unintended responses to a medicinal product related to any dose. A SR was defined as an AR observed and reported under the conditions (symptom and onset) prelisted (i.e., solicited) in the eCRF and considered as related to vaccination. Solicited systemic reactions included fever, headache, malaise, myalgia, and asthenia. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category.
End point type	Secondary
End point timeframe:	Within 14 days after each vaccination (1, 2, and 3)

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	348	348	352	
Units: subjects				
Post-vacc. 1: Fever (n=347,347,352)	10	8	13	
Post-vacc. 1: Headache (n=347,347,352)	90	83	84	
Post-vacc. 1: Malaise (n=347,347,352)	74	60	61	
Post-vacc. 1: Myalgia (n=347,347,352)	67	55	48	
Post-vacc. 1: Asthenia (n=347,347,352)	63	52	45	

Post-vacc. 2: Fever (n=332,327,330)	12	7	12	
Post-vacc. 2: Headache (n=332,328,332)	54	55	53	
Post-vacc. 2: Malaise (n=332,328,332)	50	44	47	
Post-vacc. 2: Myalgia (n=332,328,332)	49	33	35	
Post-vacc. 2: Asthenia (n=332,328,332)	40	30	33	
Post-vacc. 3: Fever (n=324,317,317)	9	8	9	
Post-vacc. 3: Headache (n=325,321,324)	55	47	47	
Post-vacc. 3: Malaise (n=325,321,324)	46	41	39	
Post-vacc. 3: Myalgia (n=325,321,324)	26	37	38	
Post-vacc. 3: Asthenia (n=325,321,324)	29	32	21	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-II: Number of Subjects With Solicited Injection Site Reactions Following Booster Vaccination With CYD Dengue Vaccine

End point title	STAGE-II: Number of Subjects With Solicited Injection Site Reactions Following Booster Vaccination With CYD Dengue Vaccine
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End point description:

An AR was defined as all noxious and unintended responses to a medicinal product related to any dose. A SR was defined as an AR observed and reported under the conditions (symptom and onset) prelisted (i.e., solicited) in the eCRF and considered as related to vaccination. Solicited injection site reaction was an AR at and around the injection site that included pain, erythema, and swelling. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary
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End point timeframe:

Within 7 days after CYD booster vaccination

End point values	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	59	62	53
Units: subjects				
Pain (n=55,59,62,53,54,52)	6	7	11	7
Erythema (n=55,59,62,53,54,52)	0	0	0	0
Swelling (n=55,59,62,53,54,52)	0	0	0	0

End point values	STAGE-II Group 2b: Placebo + CYD	STAGE-II Group 3b: Placebo + CYD		
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	+ CYD Booster (2 Years)	+ CYD Booster (2 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	53		
Units: subjects				
Pain (n=55,59,62,53,54,52)	12	10		
Erythema (n=55,59,62,53,54,52)	1	0		
Swelling (n=55,59,62,53,54,52)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-II: Number of Subjects With Solicited Systemic Reactions Following Booster Vaccination With CYD Dengue Vaccine

End point title	STAGE-II: Number of Subjects With Solicited Systemic Reactions Following Booster Vaccination With CYD Dengue Vaccine
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End point description:

An AR was defined as all noxious and unintended responses to a medicinal product related to any dose. A SR was defined as an AR observed and reported under the conditions (symptom and onset) prelisted (i.e., solicited) in the eCRF and considered as related to vaccination. Solicited systemic reactions included fever, headache, malaise, myalgia, and asthenia. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category.

End point type	Secondary
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End point timeframe:

Within 14 days after CYD booster vaccination

End point values	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	59	62	53
Units: subjects				
Fever (n=55,59,62,53,54,51)	1	0	1	2
Headache (n=55,59,62,53,54,52)	5	11	6	7
Malaise (n=55,59,62,53,54,52)	5	9	7	7
Myalgia (n=55,59,62,53,54,52)	5	8	9	9
Asthenia (n=55,59,62,53,54,52)	4	6	6	7

End point values	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)		
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Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	53		
Units: subjects				
Fever (n=55,59,62,53,54,51)	2	0		
Headache (n=55,59,62,53,54,52)	11	7		
Malaise (n=55,59,62,53,54,52)	9	5		
Myalgia (n=55,59,62,53,54,52)	12	6		
Asthenia (n=55,59,62,53,54,52)	9	3		

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-I: Number of Subjects Reporting Unsolicited Adverse Events Following Vaccination With CYD Dengue Vaccine or Placebo

End point title	STAGE-I: Number of Subjects Reporting Unsolicited Adverse Events Following Vaccination With CYD Dengue Vaccine or Placebo
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End point description:

An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An unsolicited AE was an observed AE that does not fulfill the conditions prelisted in the eCRF in terms of diagnosis and/or onset post-vaccination. Analysis was performed on SafAS.

End point type	Secondary
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End point timeframe:

Within 28 days after any vaccination (1, 2, or 3)

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	348	348	352	
Units: subjects	73	94	75	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-II: Number of Subjects Reporting Unsolicited Adverse Events Following Booster Vaccination With CYD Dengue Vaccine

End point title	STAGE-II: Number of Subjects Reporting Unsolicited Adverse Events Following Booster Vaccination With CYD Dengue Vaccine
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End point description:

An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory finding,

for example), symptom or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An unsolicited AE was an observed AE that does not fulfill the conditions prelisted in the eCRF in terms of diagnosis and/or onset post-vaccination. Analysis was performed on SafAS.

End point type	Secondary
End point timeframe:	
Within 28 days after CYD booster Vaccination	

End point values	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	59	62	53
Units: subjects	1	3	5	3

End point values	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	53		
Units: subjects	2	4		

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-I: Number of Subjects Reporting Serious Adverse Events Including Serious Adverse Event of Special Interests Following Vaccination With CYD Dengue Vaccine or Placebo

End point title	STAGE-I: Number of Subjects Reporting Serious Adverse Events Including Serious Adverse Event of Special Interests Following Vaccination With CYD Dengue Vaccine or Placebo
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End point description:

An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was congenital anomaly/birth defect, or was an important medical event. AESI were AEs that were considered by the Sponsor to be relevant for the monitoring of the safety profile of the investigational vaccine. Analysis was performed on SafAS.

End point type	Secondary
End point timeframe:	
From Day 0 (post vaccination) up to 12 months after last vaccination in STAGE-I (i.e., up to 24 months)	

End point values	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	348	348	352	
Units: subjects				
SAE	14	26	18	
Serious AESI	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: STAGE-II: Number of Subjects Reporting Serious Adverse Events Including Serious Adverse Events Special Interest Following Booster Vaccination With CYD Dengue Vaccine

End point title	STAGE-II: Number of Subjects Reporting Serious Adverse Events Including Serious Adverse Events Special Interest Following Booster Vaccination With CYD Dengue Vaccine
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End point description:

An AE was defined as any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was congenital anomaly/birth defect, or was an important medical event. AESI were AEs that were considered by the Sponsor to be relevant for the monitoring of the safety profile of the investigational vaccine. Analysis was performed on SafAS.

End point type	Secondary
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End point timeframe:

From Month 25 up to 6 months after CYD booster injection (either at 1 year or 2 year) (i.e., up to 30 months for Groups 1a, 2a, and 3a and up to 42 months for Groups 1b, 2b, and 3b)

End point values	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	55	59	62	53
Units: subjects				
SAE	3	0	2	2
Serious AESI	0	0	0	0

End point values	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	53		
Units: subjects				
SAE	0	1		
Serious AESI	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited non-serious AEs: Day 0 to Day 28 post any vacc. SR: within 7 & 14 days post any vacc. SAE: throughout trial (up to 24 months [STAGE-I]; up to 30 months [Groups 1a,2a,&3a]; & up to 42 months [Groups 1b,2b,&3b], i.e. 6 months after last vacc.)

Adverse event reporting additional description:

Analysis was performed on SafAS. SR was AE that was prelisted (i.e., solicited) in the eCRF and considered to be related to vaccination (adverse drug reaction). An unsolicited AE was an observed AE that did not fulfill the conditions prelisted (i.e., solicited) in the eCRF in terms of symptom and/or onset post-vaccination.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	STAGE-I Group 1: CYD Dengue Vaccine
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Reporting group description:

Subjects received 3 doses of CYD dengue vaccine 0.5 mL SC at Day 0 (Vaccination 1), Month 6 (Vaccination 2), and Month 12 (Vaccination 3).

Reporting group title	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)
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Reporting group description:

Subjects received a dose of placebo at Day 0 (Vaccination 1) along with 2 doses of CYD dengue vaccine 0.5 mL SC at Month 6 (Vaccination 2) and Month 12 (Vaccination 3).

Reporting group title	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)
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Reporting group description:

Subjects received 2 doses of placebo at Day 0 (Vaccination 1) and Month 6 (Vaccination 2) along with a dose of CYD dengue vaccine 0.5 mL SC at Month 12 (Vaccination 3).

Reporting group title	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)
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Reporting group description:

Subjects from Group 1 who received vaccination in STAGE-I; and were seropositive at Baseline received a booster dose of CYD dengue vaccine in STAGE-II at 1 year post last dose in STAGE-I (i.e. at Month 24).

Reporting group title	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)
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Reporting group description:

Subjects from Group 1 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 2 years post last dose in STAGE-I (i.e. at Month 36).

Reporting group title	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)
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Reporting group description:

Subjects from Group 2 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 1 year post last dose in STAGE-I (i.e. at Month 24).

Reporting group title	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)
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Reporting group description:

Subjects from Group 2 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 2 years post last dose in STAGE-I (i.e. at Month 36).

Reporting group title	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)
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Reporting group description:

Subjects from Group 3 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 1 year post last dose in STAGE-I (i.e. at Month

24).

Reporting group title	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)
Reporting group description:	
Subjects from Group 3 who received vaccination in STAGE-I and were seropositive at baseline received a booster injection of CYD dengue vaccine in STAGE-II at 2 years post last dose in STAGE-I (i.e. at Month 36).	

Serious adverse events	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 348 (4.02%)	26 / 348 (7.47%)	18 / 352 (5.11%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary Thyroid Cancer			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	2 / 348 (0.57%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion Spontaneous Incomplete			

subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Threatened Labour			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Food Allergy			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholin's Cyst			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysfunctional Uterine Bleeding			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine Polyp			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			

subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Animal Bite			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm Fracture			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gun Shot Wound			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Head Injury			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw Fracture			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Radius Fracture			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road Traffic Accident			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal Burn			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Branchial Cyst			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Food Poisoning			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Toxic Skin Eruption			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Colic			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endocrine disorders			
Thyroid Cyst			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Disc Degeneration			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological Fracture			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 348 (0.29%)	4 / 348 (1.15%)	3 / 352 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea Infectious			

subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin Abscess			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Staphylococcal			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	1 / 348 (0.29%)	0 / 348 (0.00%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			

subjects affected / exposed	0 / 348 (0.00%)	0 / 348 (0.00%)	1 / 352 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 348 (0.00%)	1 / 348 (0.29%)	0 / 352 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 55 (5.45%)	2 / 53 (3.77%)	0 / 59 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary Thyroid Cancer			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion Spontaneous Incomplete			

subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Threatened Labour			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Food Allergy			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholin's Cyst			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysfunctional Uterine Bleeding			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine Polyp			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			

subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Animal Bite			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm Fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gun Shot Wound			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw Fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Radius Fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road Traffic Accident			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal Burn			
subjects affected / exposed	1 / 55 (1.82%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Branchial Cyst			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 55 (0.00%)	1 / 53 (1.89%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Food Poisoning			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Toxic Skin Eruption			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Colic			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endocrine disorders			
Thyroid Cyst			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Disc Degeneration			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological Fracture			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 55 (1.82%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea Infectious			

subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin Abscess			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Staphylococcal			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 55 (0.00%)	1 / 53 (1.89%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			

subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 55 (0.00%)	0 / 53 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)	2 / 62 (3.23%)	1 / 53 (1.89%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary Thyroid Cancer			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion Spontaneous Incomplete			

subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Threatened Labour			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Food Allergy			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholin's Cyst			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysfunctional Uterine Bleeding			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine Polyp			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			

subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Animal Bite			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm Fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 62 (1.61%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gun Shot Wound			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw Fracture			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Radius Fracture			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road Traffic Accident			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal Burn			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Branchial Cyst			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Food Poisoning			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Toxic Skin Eruption			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus Urinary			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Colic			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endocrine disorders			
Thyroid Cyst			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral Disc Degeneration			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological Fracture			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid Arthritis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea Infectious			

subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin Abscess			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis A			
subjects affected / exposed	0 / 56 (0.00%)	1 / 62 (1.61%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Staphylococcal			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			

subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 56 (0.00%)	0 / 62 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	STAGE-I Group 1: CYD Dengue Vaccine	STAGE-I Group 2: Placebo + CYD Dengue Vaccine (Months 6,12)	STAGE-I Group 3: Placebo + CYD Dengue Vaccine (Month 12)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	203 / 348 (58.33%)	189 / 348 (54.31%)	182 / 352 (51.70%)
Nervous system disorders			
Headache	Additional description: Events of headache that occurred after 14 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	129 / 348 (37.07%)	123 / 348 (35.34%)	124 / 352 (35.23%)
occurrences (all)	201	190	184
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	98 / 348 (28.16%)	80 / 348 (22.99%)	71 / 352 (20.17%)
occurrences (all)	133	114	100
Fever			
subjects affected / exposed	29 / 348 (8.33%)	21 / 348 (6.03%)	31 / 352 (8.81%)
occurrences (all)	31	23	34
Injection Site Pain			
subjects affected / exposed	109 / 348 (31.32%)	114 / 348 (32.76%)	97 / 352 (27.56%)
occurrences (all)	154	164	146
Malaise	Additional description: Events of malaise that occurred after 14 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	114 / 348 (32.76%)	98 / 348 (28.16%)	103 / 352 (29.26%)
occurrences (all)	170	146	148
Musculoskeletal and connective tissue disorders			

Myalgia	Additional description: Events of myalgia that occurred after 14 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	110 / 348 (31.61%)	92 / 348 (26.44%)	87 / 352 (24.72%)
occurrences (all)	143	126	112

Non-serious adverse events	STAGE-II Group 1a: CYD Vaccine + CYD Booster Vaccine (1 Year)	STAGE-II Group 1b: CYD Vaccine + CYD Booster Vaccine (2 Years)	STAGE-II Group 2a: Placebo + CYD + CYD Booster (1 Year)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 55 (18.18%)	13 / 53 (24.53%)	15 / 59 (25.42%)
Nervous system disorders	Additional description: Events of headache that occurred after 14 days post-vaccination were considered as unsolicited AE.		
Headache			
subjects affected / exposed	5 / 55 (9.09%)	7 / 53 (13.21%)	11 / 59 (18.64%)
occurrences (all)	5	7	11
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 55 (7.27%)	7 / 53 (13.21%)	6 / 59 (10.17%)
occurrences (all)	4	7	6
Fever			
subjects affected / exposed	1 / 55 (1.82%)	2 / 53 (3.77%)	0 / 59 (0.00%)
occurrences (all)	1	2	0
Injection Site Pain			
subjects affected / exposed	6 / 55 (10.91%)	7 / 53 (13.21%)	7 / 59 (11.86%)
occurrences (all)	6	7	7
Malaise	Additional description: Events of malaise that occurred after 14 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	5 / 55 (9.09%)	7 / 53 (13.21%)	9 / 59 (15.25%)
occurrences (all)	5	7	9
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Events of myalgia that occurred after 14 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	5 / 55 (9.09%)	9 / 53 (16.98%)	8 / 59 (13.56%)
occurrences (all)	5	9	8

Non-serious adverse events	STAGE-II Group 2b: Placebo + CYD + CYD Booster (2 Years)	STAGE-II Group 3a: Placebo + CYD + CYD Booster (1 Year)	STAGE-II Group 3b: Placebo + CYD + CYD Booster (2 Years)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 56 (35.71%)	18 / 62 (29.03%)	15 / 53 (28.30%)
Nervous system disorders			

Headache	Additional description: Events of headache that occurred after 14 days post-vaccination were considered as unsolicited AE.		
	subjects affected / exposed	12 / 56 (21.43%)	7 / 62 (11.29%)
	occurrences (all)	12	7
General disorders and administration site conditions			
Asthenia			
	subjects affected / exposed	9 / 56 (16.07%)	6 / 62 (9.68%)
	occurrences (all)	9	6
Fever			
	subjects affected / exposed	2 / 56 (3.57%)	1 / 62 (1.61%)
	occurrences (all)	2	1
Injection Site Pain			
	subjects affected / exposed	12 / 56 (21.43%)	11 / 62 (17.74%)
	occurrences (all)	12	11
Malaise			
Additional description: Events of malaise that occurred after 14 days post-vaccination were considered as unsolicited AE.			
	subjects affected / exposed	9 / 56 (16.07%)	7 / 62 (11.29%)
	occurrences (all)	9	7
Musculoskeletal and connective tissue disorders			
Myalgia			
Additional description: Events of myalgia that occurred after 14 days post-vaccination were considered as unsolicited AE.			
	subjects affected / exposed	12 / 56 (21.43%)	9 / 62 (14.52%)
	occurrences (all)	12	9
			6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2017	As per Independent Data Monitoring Committee recommendation not to further vaccinate subjects not previously infected by dengue, Sanofi Pasteur amended the study protocol so that only subjects assessed as previously infected by dengue before receiving the first CYD dengue vaccine injection were eligible to receive any further dose of the CYD dengue vaccine in the study. All subjects were informed about their serostatus at Baseline. Moreover, all subjects were asked about their willingness to continue participating in this study by signing an updated informed consent form and/or assent form, as applicable. Subjects assessed as dengue seropositive confirmed their participation in the study and continued to be eligible to receive the booster injection at Year 1 or Year 2. Subjects classified as seronegative at Baseline were only able to continue in the study for safety follow-up and for the evaluation of Ab persistence at Year 1. It consisted in the addition of a co-primary objective, to determine the non-inferiority of the immune response at both 28 days and 1 year after the last dose (3 doses versus 2 doses schedule). Non-inferiority tests between Group 3 and Group 1 became no longer applicable. Rather, the immunogenicity of the 1-dose regimen was described as part of the additional objectives. Addition of a visit to the study centers for subjects from Subgroup b who did not have such a visit planned in the original protocol. It required subjects and/or their parents/legally accepted representatives to provide their written consent. Subjects assigned to Subgroup b were asked to provide a blood sample at 1 year post last primary series injection, regardless of whether or not they were eligible to receive a booster vaccination.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported