Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate Efficacy, Safety, and Immunogenicity of V260 in Healthy Chinese Infants

Summary

EudraCT number	2016-005159-25
Trial protocol	Outside EU/EEA
Global end of trial date	11 June 2015

Results information

Result version number	v1 (current)
This version publication date	03 August 2018
First version publication date	03 August 2018

Trial information

Trial identification

Sponsor protocol code	V260-024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02062385
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	11 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study assessed the efficacy, safety, and immunogenicity of a 3-dose regimen of RotaTeq™ (V260) in healthy Chinese infants. Approximately 4040 participants at least 6 weeks and up to 12 weeks of age at the time of the first vaccination with V260 or placebo were to be enrolled and randomized (1:1) to receive either V260 or placebo. Participants were also to receive the routine China Expanded Program on Immunization (EPI) vaccines (oral poliovirus vaccine [OPV] and diphtheria, tetanus, and acellular pertussis vaccine [DTaP]) either staggered or concomitantly with V260 or placebo. All participants were followed for efficacy and safety. Immune responses to OPV and DTaP were evaluated in a subset of participants. The primary hypothesis of the study states that V260 will be efficacious in preventing any severity of rotavirus gastroenteritis as compared with placebo.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 May 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 4040
Worldwide total number of subjects	4040
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)	4040
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 4173 participants were screened, 4040 were randomized, and 4037 received at least one dose of study vaccination.

Pre-assignment

Screening details:

The study enrolled healthy Chinese infants.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	V260 with Staggered EPI

Arm description:

V260 administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered China Expanded Program on Immunization (EPI) as follows: Oral poliovirus vaccine (OPV) administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and diphtheria, tetanus, acellular pertussis vaccine (DTaP) administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months.

Arm type	Experimental
Investigational medicinal product name	V260
Investigational medicinal product code	
Other name	RotaTeq™; live, oral, pentavalent rotavirus vaccine
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL oral solution

Investigational medicinal product name	Diphtheria, tetanus, acellular pertussis vaccine (DTaP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 intramuscular injection

Investigational medicinal product name	Oral poliovirus vaccine (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

1 gram oral solution

Arm title	Placebo with Staggered EPI

Arm description:

Placebo administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered EPI as follows: OPV administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL oral solution

Investigational medicinal product name	Oral poliovirus vaccine (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

1 gram oral solution

Investigational medicinal product name	Diphtheria, tetanus, acellular pertussis vaccine (DTaP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 intramuscular injection

Arm title	V260 with Concomitant EPI

Arm description:

V260 administered as a 2 mL oral solution at age ~2, 3, and 4 months, and concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Arm type	Experimental
Investigational medicinal product name	V260
Investigational medicinal product code	
Other name	RotaTeq™; live, oral, pentavalent rotavirus vaccine
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mL oral solution

Investigational medicinal product name	Oral poliovirus vaccine (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

1 gram oral solution

Investigational medicinal product name	Diphtheria, tetanus, acellular pertussis vaccine (DTaP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 intramuscular injection

Arm title	Placebo with Concomitant EPI

Arm description:

Placebo administered as a 2 mL oral solution at age ~2, 3, and 4 months, and concomitant EPI as

follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details: 2 mL oral solution	
Investigational medicinal product name	Oral poliovirus vaccine (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details: 1 gram oral solution	
Investigational medicinal product name	Diphtheria, tetanus, acellular pertussis vaccine (DTaP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: 0.5 intramuscular injection	

Number of subjects in period 1	V260 with Staggered EPI	Placebo with Staggered EPI	V260 with Concomitant EPI
Started	1620	1620	400
Received Vaccination 1	1618	1619	400
Received Vaccination 2	1554	1566	392
Received Vaccination 3	1543	1554 [1]	389
Completed	1542	1555	388
Not completed	78	65	12
Withdrawn by parent/guardian	46	41	9
Adverse event, serious fatal	-	-	-
Adverse event, non-fatal	19	13	1
Moved	10	11	1
Lost to follow-up	-	-	1
Incomplete EPI by database lock	2	-	-
Protocol deviation	1	-	-

Number of subjects in period 1	Placebo with Concomitant EPI
Started	400
Received Vaccination 1	400
Received Vaccination 2	393

Received Vaccination 3	392
Completed	391
Not completed	9
Withdrawn by parent/guardian	8
Adverse event, serious fatal	1
Adverse event, non-fatal	-
Moved	-
Lost to follow-up	-
Incomplete EPI by database lock	-
Protocol deviation	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: One participant did not receive the third vaccination but continued in the study.

Baseline characteristics

Reporting groups	
Reporting group title	V260 with Staggered EPI
Reporting group description:	
V260 administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered China Expanded Program on Immunization (EPI) as follows: Oral poliovirus vaccine (OPV) administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and diphtheria, tetanus, acellular pertussis vaccine (DTaP) administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months.	
Reporting group title	Placebo with Staggered EPI
Reporting group description:	
Placebo administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered EPI as follows: OPV administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months.	
Reporting group title	V260 with Concomitant EPI
Reporting group description:	
V260 administered as a 2 mL oral solution at age ~2, 3, and 4 months, and concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.	
Reporting group title	Placebo with Concomitant EPI
Reporting group description:	
Placebo administered as a 2 mL oral solution at age ~2, 3, and 4 months, and concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.	

Reporting group values	V260 with Staggered EPI	Placebo with Staggered EPI	V260 with Concomitant EPI
Number of subjects	1620	1620	400
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	1620	1620	400
Age Continuous Units: days			
arithmetic mean	57.5	57.2	68.3
standard deviation	± 10.0	± 9.7	± 5.7
Gender, Male/Female Units: Subjects			
Female	806	775	185
Male	814	845	215

Reporting group values	Placebo with Concomitant EPI	Total	
Number of subjects	400	4040	
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	400	4040	
Age Continuous Units: days			
arithmetic mean	68.5		
standard deviation	± 5.7	-	

Gender, Male/Female Units: Subjects			
Female	183	1949	
Male	217	2091	

End points

End points reporting groups

Reporting group title	V260 with Staggered EPI

Reporting group description:

V260 administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered China Expanded Program on Immunization (EPI) as follows: Oral poliovirus vaccine (OPV) administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and diphtheria, tetanus, acellular pertussis vaccine (DTaP) administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months.

Reporting group title	Placebo with Staggered EPI

Reporting group description:

Placebo administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered EPI as follows: OPV administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months.

Reporting group title	V260 with Concomitant EPI

Reporting group description:

V260 administered as a 2 mL oral solution at age ~2, 3, and 4 months, and concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Reporting group title	Placebo with Concomitant EPI

Reporting group description:

Placebo administered as a 2 mL oral solution at age ~2, 3, and 4 months, and concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Subject analysis set title	V260 with Staggered or Concomitant EPI
Subject analysis set type	Per protocol

Subject analysis set description:

V260 administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered EPI as follows: OPV administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months OR concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Subject analysis set title	Placebo with Staggered or Concomitant EPI
Subject analysis set type	Per protocol

Subject analysis set description:

Placebo administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered EPI as follows: OPV administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months OR concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Subject analysis set title	V260 with Staggered or Concomitant EPI
Subject analysis set type	Safety analysis

Subject analysis set description:

V260 administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered EPI as follows: OPV administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months OR concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Subject analysis set title	Placebo with Staggered or Concomitant EPI
Subject analysis set type	Safety analysis

Subject analysis set description:

Placebo administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered EPI as follows: OPV administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months OR concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Primary: Number of Participants with Any Severity of Rotavirus Gastroenteritis

End point title	Number of Participants with Any Severity of Rotavirus Gastroenteritis

End point description:

The number of participants with rotavirus gastroenteritis (RVGE) caused by naturally-occurring wild-type rotavirus (regardless of serotype or disease severity) was assessed. The case definition of RVGE included 1) 3 or more watery or looser-than-normal stools within a 24-hour period and/or forceful vomiting, and 2) naturally-occurring wild-type rotavirus must be detected in a stool specimen taken within 7 days after the onset of symptoms. The population was participants who were vaccinated in either the staggered EPI or concomitant EPI groups, were not protocol violators, and were classified as evaluable for RVGE according to the per-protocol case definition.

End point type	Primary

End point timeframe:

From 14 days after the third dose of V260 or placebo through the first rotavirus season (up to 15 months)

End point values	V260 with Staggered or Concomitant EPI	Placebo with Staggered or Concomitant EPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1927	1937		
Units: Participants	34	109		

Statistical analyses

Statistical analysis title	Vaccine Efficacy
Comparison groups	V260 with Staggered or Concomitant EPI v Placebo with Staggered or Concomitant EPI
Number of subjects included in analysis	3864
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.001 [2]
Method	Poisson distribution
Parameter estimate	Vaccine efficacy
Point estimate	69.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	54.5
upper limit	79.7

Notes:

[1] - V260 will be considered efficacious if the lower bound of the two-sided confidence interval for efficacy is >0% at the final analysis

[2] - To calculate the confidence interval and associated p-value, an exact conditional method based on a Poisson distribution was used.

Secondary: Percentage of Participants with Elevated Temperature

End point title	Percentage of Participants with Elevated Temperature

End point description:

Elevated temperature (temperature >=37.5°C axillary or equivalent) was noted by the guardian and

recorded on the Vaccination Report Card during Day 1 to Day 14 after each dose of vaccination. Elevated temperature reported by the guardian was also collected as an adverse event (pyrexia) during Day 15 to Day 30 after each dose of vaccination. The percentage of participants with axillary temperature >=37.5 °C or an adverse event of pyrexia was assessed. The population was All Subjects as Treated with follow-up specific to the endpoint.

End point type	Secondary

End point timeframe:

Up to 30 days after any dose of V260 or Placebo

End point values	V260 with Staggered or Concomitant EPI	Placebo with Staggered or Concomitant EPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2015	2019		
Units: Percentage of participants				
number (not applicable)	21.84	22.83		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Vomiting or Diarrhea

End point title	Percentage of Participants with Vomiting or Diarrhea

End point description:

Episodes of vomiting and diarrhea were noted by the guardian and recorded on the Vaccination Record Card during Day 1 to Day 14 after each dose of vaccination. Vomiting and diarrhea reported by the guardian were also collected as an adverse event during Day 15 to Day 30 after any dose of vaccination. The percentage of participants with an episode or an adverse event of vomiting or diarrhea was assessed. The population was All Subjects as Treated with follow-up specific to the endpoint.

End point type	Secondary

End point timeframe:

Up to 30 days after any dose of V260 or Placebo

End point values	V260 with Staggered or Concomitant EPI	Placebo with Staggered or Concomitant EPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2015	2019		
Units: Percentage of participants				
number (not applicable)				
Vomiting	2.68	3.52		
Diarrhea	20.15	20.11		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Intussusception

End point title	Percentage of Participants with Intussusception

End point description:

Episodes of intussusception were collected from the time of written consent until the end of study. The percentage of participants with an episode of intussusception was assessed. The population was All Subjects as Treated with follow-up specific to the endpoint.

End point type	Secondary

End point timeframe:

Up to 15 months

End point values	V260 with Staggered or Concomitant EPI	Placebo with Staggered or Concomitant EPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2015	2019		
Units: Percentage of participants				
number (not applicable)	0.10	0.00		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Severe Rotavirus Gastroenteritis

End point title	Number of Participants with Severe Rotavirus Gastroenteritis

End point description:

The number of participants with severe rotavirus gastroenteritis (RVGE) caused by naturally-occurring wildtype rotavirus (regardless of serotype or disease severity) was assessed. The case definition of RVGE included 1) 3 or more watery or looser-than-normal stools within a 24-hour period and/or forceful vomiting, and 2) naturally-occurring wild-type rotavirus must be detected in a stool specimen taken within 7 days after the onset of symptoms. Severe RVGE was defined as >=11 on the Vesikari Scoring System, a composite of the seven parameters related to symptoms and treatment with an overall range from 0 to 20. The population was participants who were vaccinated in either the staggered EPI or concomitant EPI groups, were not protocol violators, and were classified as evaluable for RVGE according to the per-protocol case definition.

End point type	Secondary

End point timeframe:

From 14 days after the third dose of V260 or placebo through the first rotavirus season (up to 15 months)

End point values	V260 with Staggered or Concomitant EPI	Placebo with Staggered or Concomitant EPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1926[3]	1937		
Units: Participants	11	52		

Notes:

[3] - 1 participant was excluded because the severity of RVGE was unknown

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved Seroprotection Against Poliovirus Type 1, 2, or 3

End point title	Percentage of Participants who Achieved Seroprotection Against Poliovirus Type 1, 2, or 3[4]

End point description:

The percentage of participants who achieved seroprotection against poliovirus Type 1, 2, or 3 was assessed. Seroprotection was defined as a neutralizing antibody titer >=1:8. This outcome was evaluated only in participants receiving concomitant administration of V260 and OPV. The population was participants in the concomitant EPI groups who receive their scheduled doses of OPV without intervening disease specific to the antigen before the blood sample collection postdose 3, adhere to the guidelines for administration of vaccine, and have valid values available for analysis within specified day ranges.

End point type	Secondary

End point timeframe:

Baseline and between 28 and 56 days after the third OPV vaccination

Notes:

[4] - 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: This endpoint was evaluated only in participants receiving concomitant administration of V260 and OPV.

End point values	V260 with Concomitant EPI	Placebo with Concomitant EPI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	192		
Units: Percentage of participants				
number (confidence interval 95%)				
Poliovirus Type 1: Baseline, n=186, 190	44.09 (36.83 to 51.54)	38.95 (31.97 to 46.27)		
Poliovirus Type 1: Post OPV #3, n=187, 192	98.93 (96.19 to 99.87)	100.00 (98.10 to 100.00)		
Poliovirus Type 2: Baseline, n=186, 190	44.09 (36.83 to 51.54)	41.58 (34.49 to 48.94)		
Poliovirus Type 2: Post OPV #3, n=187, 192	100.00 (98.05 to 100.00)	100.00 (98.10 to 100.00)		
Poliovirus Type 3: Baseline, n=186, 190	25.27 (19.20 to 32.15)	21.05 (15.49 to 27.54)		
Poliovirus Type 3: Post OPV #3, n=187, 192	98.93 (96.19 to 99.87)	98.96 (96.29 to 99.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Any Adverse Event

End point title	Percentage of Participants with Any Adverse Event

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening of a preexisting condition that is temporally associated with the use of the sponsor's product, is also an adverse event. The population was All Subjects as Treated with safety follow-up.

End point type	Secondary

End point timeframe:

Up to 30 days after any dose of V260 or Placebo

End point values	V260 with Staggered or Concomitant EPI	Placebo with Staggered or Concomitant EPI		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2015	2019		
Units: Percentage of participants				
number (not applicable)	53.5	53.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Seropositive to Diphtheria, Pertussis, or Tetanus Antigens

End point title	Percentage of Participants Seropositive to Diphtheria, Pertussis, or Tetanus Antigens[5]

End point description:

The percentage of participants seropositive to diphtheria, pertussis, or tetanus antigens was assessed. Seropositive was defined as the following: 1) anti-diphtheria antibody titers >=0.1 International Units (IU)/mL, 2) anti-tetanus antibody titers >=0.1 IU/mL, 3) antipertussis toxin antibody titers >=20 Enzyme-linked Immunosorbent Assay (ELISA) Units (EU)/mL, 4) anti-pertussis filamentous hemagglutinin (FHA) antibody titers >=20 EU/mL. This outcome was evaluated only in participants receiving concomitant administration of V260 or placebo and EPI. The population was participants in the concomitant EPI groups who receive their scheduled doses of DTaP without intervening disease specific to the antigen before the blood sample collection postdose 3, adhere to the guidelines for administration of vaccine, and have valid values available for analysis within specified day ranges.

End point type	Secondary

End point timeframe:

Baseline and between 28 and 51 days after the third DTaP vaccination

Notes:

[5] - 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: This endpoint was evaluated only in participants receiving concomitant administration of V260 or placebo and EPI.

End point values	V260 with Concomitant EPI	Placebo with Concomitant EPI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	194		
Units: Percentage of participants				
number (confidence interval 95%)				
Diphtheria: Baseline, n=181, 186	3.31 (1.23 to 7.08)	2.69 (0.88 to 6.16)		
Diphtheria: Post DTaP #3, n=187, 194	99.47 (97.06 to 99.99)	99.48 (97.16 to 99.99)		
Pertussis FHA: Baseline, n=181, 186	0.00 (0.00 to 2.02)	0.00 (0.00 to 1.96)		
Pertussis FHA: Post DTaP #3, n=187, 194	44.92 (37.65 to 52.35)	43.81 (36.72 to 51.10)		
Pertussis Toxin: Baseline, n=181, 186	1.66 (0.34 to 4.77)	1.08 (0.13 to 3.83)		
Pertussis Toxin, Post DTaP #3, n=187, 194	95.19 (91.06 to 97.78)	94.33 (90.08 to 97.14)		
Tetanus: Baseline, n=181, 186	12.15 (7.78 to 17.82)	12.37 (8.00 to 17.97)		
Tetanus: Post DTaP #3, n=187, 194	100.00 (98.05 to 100.00)	100.00 (98.12 to 100.00)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events: up to 30 days after any V260 or placebo vaccination; Serious Adverse Events: from the time of written consent until the end of the study (up to 15 months)

Adverse event reporting additional description:

The at-risk population was All Subjects as Treated. Adverse events are reported for participants who received V260 or placebo without regard to staggered or concomitant EPI administration.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Placebo with Staggered or Concomitant EPI

Reporting group description:

Placebo administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered EPI as follows: OPV administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months OR concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Reporting group title	V260 with Staggered or Concomitant EPI

Reporting group description:

V260 administered as a 2 mL oral solution at age ~2, 3, and 4 months, and staggered EPI as follows: OPV administered as a 1 g oral solution at age ~2.5, 3.5, and 4.5 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3.5, 4.5, and 5.5 months OR concomitant EPI as follows: OPV administered as a 1 g oral solution at age ~2, 3, and 4 months, and DTaP administered as a 0.5 mL intramuscular injection at age ~3, 4, and 5 months.

Serious adverse events	Placebo with Staggered or Concomitant EPI	V260 with Staggered or Concomitant EPI	
Total subjects affected by serious adverse events			
subjects affected / exposed	338 / 2019 (16.74%)	339 / 2015 (16.82%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Developmental delay			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Transient hypogammaglobulinaemia of infancy			

subjects affected / exposed	1 / 2019 (0.05%)	2 / 2015 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	9 / 2019 (0.45%)	17 / 2015 (0.84%)	
occurrences causally related to treatment / all	0 / 9	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye contusion			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Talipes			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalassaemia			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thalassaemia beta			

subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular septal defect			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	1 / 2019 (0.05%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Central nervous system lesion			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	3 / 2019 (0.15%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 2019 (0.05%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Granulocytopenia			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 2019 (0.45%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	41 / 2019 (2.03%)	47 / 2015 (2.33%)	
occurrences causally related to treatment / all	0 / 42	0 / 52	
deaths causally related to treatment / all	0 / 0	0 / 0	
Functional gastrointestinal disorder			
subjects affected / exposed	2 / 2019 (0.10%)	2 / 2015 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intestinal obstruction			
subjects affected / exposed	6 / 2019 (0.30%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	1 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	0 / 2019 (0.00%)	2 / 2015 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis diaper			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 2019 (0.00%)	2 / 2015 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rickets			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acute tonsillitis			

subjects affected / exposed	5 / 2019 (0.25%)	9 / 2015 (0.45%)	
occurrences causally related to treatment / all	0 / 5	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 2019 (0.05%)	2 / 2015 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	101 / 2019 (5.00%)	84 / 2015 (4.17%)	
occurrences causally related to treatment / all	0 / 108	0 / 89	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	141 / 2019 (6.98%)	129 / 2015 (6.40%)	
occurrences causally related to treatment / all	0 / 158	0 / 144	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	3 / 2019 (0.15%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	21 / 2019 (1.04%)	20 / 2015 (0.99%)	
occurrences causally related to treatment / all	1 / 22	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			

subjects affected / exposed	1 / 2019 (0.05%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	3 / 2019 (0.15%)	3 / 2015 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis bacterial			
subjects affected / exposed	1 / 2019 (0.05%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	24 / 2019 (1.19%)	7 / 2015 (0.35%)	
occurrences causally related to treatment / all	1 / 24	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis shigella			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingivitis			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	10 / 2019 (0.50%)	19 / 2015 (0.94%)	
occurrences causally related to treatment / all	0 / 10	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpangina			

subjects affected / exposed	2 / 2019 (0.10%)	13 / 2015 (0.65%)	
occurrences causally related to treatment / all	0 / 2	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes virus infection			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Omphalitis			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	3 / 2019 (0.15%)	2 / 2015 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral infection			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			

subjects affected / exposed	23 / 2019 (1.14%)	21 / 2015 (1.04%)	
occurrences causally related to treatment / all	0 / 23	0 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis bacterial			
subjects affected / exposed	5 / 2019 (0.25%)	2 / 2015 (0.10%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	14 / 2019 (0.69%)	30 / 2015 (1.49%)	
occurrences causally related to treatment / all	0 / 14	0 / 34	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 2019 (0.05%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis bacterial			
subjects affected / exposed	3 / 2019 (0.15%)	3 / 2015 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxoplasmosis			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	18 / 2019 (0.89%)	16 / 2015 (0.79%)	
occurrences causally related to treatment / all	0 / 19	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	0 / 2019 (0.00%)	1 / 2015 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 2019 (0.05%)	0 / 2015 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo with Staggered or Concomitant EPI	V260 with Staggered or Concomitant EPI	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	931 / 2019 (46.11%)	938 / 2015 (46.55%)	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	419 / 2019 (20.75%)	414 / 2015 (20.55%)	
occurrences (all)	481	492	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	406 / 2019 (20.11%)	406 / 2015 (20.15%)	
occurrences (all)	504	487	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	92 / 2019 (4.56%)	115 / 2015 (5.71%)	
occurrences (all)	109	133	
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	233 / 2019 (11.54%)	228 / 2015 (11.32%)	
occurrences (all)	268	248	
Upper respiratory tract infection			
subjects affected / exposed	103 / 2019 (5.10%)	91 / 2015 (4.52%)	
occurrences (all)	114	98	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2014	Amendment 1: the participant cohorts were reorganized as "Staggered Use" and Concomitant Use" groups; randomization ratio was clarified as 1:1 for V260:Placebo; sample sizes for study subgroups were changed; clarified that OPV and DTaP will be provided through routine health care (China EPI); changes to the timing and volumes of certain blood draws; changes to certain AE collection times; clarification of temperature assessment method; updated power calculations to reflect reduced subgroup sample sizes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported