Clinical trial results:
Post-marketing, Randomized, Open-label Study to Assess the Immunogenicity and Safety of Concomitant Administration of V260 and Diphtheria, Tetanus, Pertussis and Inactivated Poliovirus Vaccine (DTP-IPV) in Japanese Healthy Infants

Summary

EudraCT number	2017-000277-37
Trial protocol	Outside EU/EEA
Global end of trial date	06 June 2014

Results information

Result version number	v1 (current)
This version publication date	26 May 2017
First version publication date	26 May 2017

Trial information

Trial identification

Sponsor protocol code	V260-060

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01926015
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	09 September 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study evaluated the immunogenicity of DTP-IPV (TetrabikTM) with concomitant administration of RotaTeqTM (V260) in healthy Japanese infants. The hypothesis to be tested was that the antibody response rates to DTP-IPV with concomitant administration of RotaTeqTM were non-inferior to those with staggered administration of RotaTeqTM.

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	19 September 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 192
Worldwide total number of subjects	192
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)	192
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: -

Pre-assignment

Screening details:

A total of 193 participants' parents/legal guardians agreed to participate by giving written informed consent for study participation. Of these, a total of 192 participants were randomised and 190 participants received study vaccinations; 2 participants were randomised but did not receive study vaccination.

Period 1

Period 1 title	Randomisation and Overall Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Concomitant RotaTeqTM + DTP-IPV

Arm description:

RotaTeqTM (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

Arm type	Experimental
Investigational medicinal product name	RotaTeqTM
Investigational medicinal product code	
Other name	V260
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Live, oral, pentavalent vaccine containing 5 human-bovine reassortant rotavirus strains. 2 mL oral administration at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

Investigational medicinal product name	DTP-IPV
Investigational medicinal product code	
Other name	TetrabikTM
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Diphtheria, tetanus, pertussis, inactivated polio vaccine used as part of the Japanese vaccination schedule. 0.5 mL subcutaneous injection at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

Arm title	Staggered RotaTeqTM + DTP-IPV

Arm description:

RotaTeqTM (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

Arm type	Experimental
Investigational medicinal product name	RotaTeqTM
Investigational medicinal product code	
Other name	V260
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Live, oral, pentavalent vaccine containing 5 human-bovine reassortant rotavirus strains. 2 mL oral administration at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

Investigational medicinal product name	DTP-IPV
Investigational medicinal product code	
Other name	TetrabikTM
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Diphtheria, tetanus, pertussis, inactivated polio vaccine used as part of the Japanese vaccination schedule. 0.5 mL subcutaneous injection at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

Number of subjects in period 1	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV
Started	96	96
Received >=1 Vaccination	94	96
Completed	94	95
Not completed	2	1
Withdrawal By Parent/Guardian	-	1
Randomised Not Treated	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Concomitant RotaTeqTM + DTP-IPV
Reporting group description:	
RotaTeqTM (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)	
Reporting group title	Staggered RotaTeqTM + DTP-IPV
Reporting group description:	
RotaTeqTM (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)	

Reporting group values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV	Total
Number of subjects	96	96	192
Age Categorical			
Units: Subjects			
Age Continuous			
Units: weeks			
median	8	9	
full range (min-max)	6 to 10	6 to 10	-
Gender Categorical			
Units: Subjects			
Female	47	41	88
Male	49	55	104

Subject analysis sets	
Subject analysis set title	Concomitant RotaTeqTM + DTP-IPV
Subject analysis set type	Per protocol
Subject analysis set description:	
RotaTeqTM (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)	
Subject analysis set title	Staggered RotaTeqTM + DTP-IPV
Subject analysis set type	Per protocol
Subject analysis set description:	
RotaTeqTM (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)	

Reporting group values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV	
Number of subjects	93	94	
Age Categorical			
Units: Subjects			

Age Continuous Units: weeks median full range (min-max)	 8 6 to 10	 9 6 to 10	
Gender Categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Concomitant RotaTeqTM + DTP-IPV
Reporting group description:	
RotaTeqTM (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)	
Reporting group title	Staggered RotaTeqTM + DTP-IPV
Reporting group description:	
RotaTeqTM (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)	
Subject analysis set title	Concomitant RotaTeqTM + DTP-IPV
Subject analysis set type	Per protocol
Subject analysis set description:	
RotaTeqTM (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)	
Subject analysis set title	Staggered RotaTeqTM + DTP-IPV
Subject analysis set type	Per protocol
Subject analysis set description:	
RotaTeqTM (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)	

Primary: Percentage of Participants Who Achieved a Serologic Response for Diphtheria Toxin, Tetanus Toxin, Pertussis Toxin, Pertussis Filamentous Hemagglutinin (FHA) and Poliovirus (PV) Type 1/2/3

End point title	Percentage of Participants Who Achieved a Serologic Response for Diphtheria Toxin, Tetanus Toxin, Pertussis Toxin, Pertussis Filamentous Hemagglutinin (FHA) and Poliovirus (PV) Type 1/2/3
End point description:	
Participant serum was collected for determination of antibody responses. Threshold levels for serologic response were the following: Diphtheria Toxin, >=0.1 International Units (IU)/mL; Tetanus Toxin, >=0.01 IU/mL; Pertussis Toxin and Pertussis FHA, >=10 Enzyme Units (EU)/mL; Poliovirus Types 1, 2, and 3, neutralising antibody (NA) titer >=8.	
End point type	Primary
End point timeframe:	
4 to 6 weeks after the third dose of DTP-IPV	

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	93	94		
Units: Percentage of participants				
number (not applicable)				
Diphtheria Toxin >=0.1 IU/mL	100	100		
Tetanus Toxin >=0.01 IU/mL	100	100		
Pertussis Toxin >=10 EU/mL	100	100		
Pertussis FHA >=10 EU/mL	100	100		
Poliovirus Type 1 NA >=8	100	100		

Poliovirus Type 2 NA >=8	100	100		
Poliovirus Type 3 NA >=8	100	100		

Statistical analyses

Statistical analysis title	Compared Seroprotection Against Diphtheria Toxin
Comparison groups	Staggered RotaTeqTM + DTP-IPV v Concomitant RotaTeqTM + DTP-IPV
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Serologic Response Rates
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.99
upper limit	3.95

Notes:

[1] - The infection control threshhold level for seroprotection against Diphtheria Toxin is >=0.1 IU/mL. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference >=10%, is >=-0.10.

Statistical analysis title	Compared Seroprotection Against Diphtheria Toxin
Comparison groups	Concomitant RotaTeqTM + DTP-IPV v Staggered RotaTeqTM + DTP-IPV
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Serologic Response Rates
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.99
upper limit	3.95

Notes:

[2] - The infection control threshhold level for seroprotection against Tetanus Toxin is >=0.01 IU/mL. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference >=10%, is >=-0.10.

Statistical analysis title	Compared Seroprotection Against Pertussis Toxin
Comparison groups	Concomitant RotaTeqTM + DTP-IPV v Staggered RotaTeqTM + DTP-IPV

Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Serologic Response Rates
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.99
upper limit	3.95

Notes:

[3] - The infection control threshhold level for seroprotection against Pertussis Toxin is >=10 EU/mL. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference >=10%, is >=-0.10.

Statistical analysis title	Compared Seroprotection Against Pertussis FHA
Comparison groups	Concomitant RotaTeqTM + DTP-IPV v Staggered RotaTeqTM + DTP-IPV
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Serologic Response Rates
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.99
upper limit	3.95

Notes:

[4] - The infection control threshhold level for seroprotection against Pertussis FHA is >=10 EU/mL. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference >=10%, is >=-0.10.

Statistical analysis title	Compared Seroprotection Against PV Type 1
Comparison groups	Concomitant RotaTeqTM + DTP-IPV v Staggered RotaTeqTM + DTP-IPV
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Serologic Response Rates
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.99
upper limit	3.95

Notes:

[5] - The infection control threshhold level for seroprotection against PV Type 1 is neutralising antibody titer (NA) >=8. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference >=10%, is >=-0.10.

Statistical analysis title	Compared Seroprotection Against PV Type 2
Comparison groups	Concomitant RotaTeqTM + DTP-IPV v Staggered RotaTeqTM + DTP-IPV
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Serologic Response Rates
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.99
upper limit	3.95

Notes:

[6] - The infection control threshhold level for seroprotection against PV Type 2 is NA >=8. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference >=10%, is >=-0.10.

Statistical analysis title	Compared Seroprotection Against PV Type 3
Comparison groups	Concomitant RotaTeqTM + DTP-IPV v Staggered RotaTeqTM + DTP-IPV
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Serologic Response Rates
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.99
upper limit	3.95

Notes:

[7] - The infection control threshhold level for seroprotection against PV Type 3 is NA >=8. Non-inferiority of concomitant versus staggered administration requires that the lower bound of the 95% confidence interval of the percentage difference, excluding a difference >=10%, is >=-0.10.

Secondary: Percentage of Participants Reporting an Adverse Event With Incidence >=1%

End point title	Percentage of Participants Reporting an Adverse Event With Incidence >=1%

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events with an incidence >=1% in either treatment group were recorded. Each participant was counted only once within a study Period and only once Overall.

End point type	Secondary

End point timeframe:

Up to 14 days after any of the 6 study visits

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	96		
Units: Percentage of participants				
number (not applicable)	68.1	86.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Reporting an Adverse Event of Special Interest: Fever

End point title	Percentage of Participants Reporting an Adverse Event of Special Interest: Fever

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events of special interest included fever, diarrhoea, vomiting, and injection-site adverse events. The safety population included randomised participants who received >=1 dose of study vaccine and had safety follow-up. Each participant was counted only once within a study Period and only once Overall.

End point type	Secondary

End point timeframe:

Period 1 (up to 14 days after Visit 1 [V1] or V2), Period 2 (up to 14 days after V3 or V4), Period 3 (up to 14 days after V5 or V6), and Overall (up to 14 days after any visit)

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	96		
Units: Percentage of participants				
number (not applicable)				
Period 1 (up to 14 days after V1 or V2) (n=94, 96)	5.3	6.3		
Period 2 (up to 14 days after V3 or V4) (n=94, 96)	1.1	12.5		
Period 3 (up to 14 days after V5 or V6)(n=94, 95)	4.3	6.3		
Overall (up to 14 days after any visit)(n=94, 96)	10.6	22.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Reporting an Adverse Event of Special Interest: Diarrhoea

End point title	Percentage of Participants Reporting an Adverse Event of Special Interest: Diarrhoea

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events of special interest included fever, diarrhea, vomiting, and injection-site adverse events. The safety population included randomized participants who received >=1 dose of study vaccine and had safety follow-up. Each participant was counted only once within a study Period and only once Overall.

End point type	Secondary

End point timeframe:

Period 1 (up to 14 days after Visit 1 [V1] or V2), Period 2 (up to 14 days after V3 or V4), Period 3 (up to 14 days after V5 or V6), and Overall (up to 14 days after any visit)

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	96		
Units: Percentage of participants				
number (not applicable)				
Period 1 (up to 14 days after V1 or V2) (n=94, 96)	17	31.3		
Period 2 (up to 14 days after V3 or V4) (n=94, 96)	10.6	20.8		
Period 3 (up to 14 days after V5 or V6) (n=94, 95)	7.4	18.9		
Overall (up to 14 days after any visit)(n=94, 96)	25.5	46.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Reporting an Adverse Event of Special Interest: Vomiting

End point title	Percentage of Participants Reporting an Adverse Event of Special Interest: Vomiting

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events of special interest included fever, diarrhoea, vomiting, and injection-site adverse events. The safety population included randomized participants who received >=1 dose of study vaccine and had safety follow-up. Each participant was counted only once within a study Period and only once Overall.

End point type	Secondary

End point timeframe:

Period 1 (up to 14 days after Visit 1 [V1] or V2), Period 2 (up to 14 days after V3 or V4), Period 3 (up to 14 days after V5 or V6), and Overall (up to 14 days after any visit)

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	96		
Units: Percentage of participants				
number (not applicable)				
Period 1 (up to 14 days after V1 or V2) (n=94, 96)	5.3	9.4		
Period 2 (up to 14 days after V3 or V4) (n=94, 96)	3.2	6.3		
Period 3 (up to 14 days after V5 or V6) (n=94, 95)	1.1	4.2		
Overall (up to 14 days after any visit) (n=94, 96)	8.5	16.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Reporting an Adverse Event of Special Interest: Injection-site Adverse Events

End point title	Percentage of Participants Reporting an Adverse Event of Special Interest: Injection-site Adverse Events

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered study drug and which does not necessarily have to have a causal relationship with this treatment. Any worsening of a preexisting condition that is temporally associated with the use of the study drug is also an adverse event. Adverse events of special interest included fever, diarrhoea, vomiting, and injection-site adverse events. The safety population included randomized participants who received >=1 dose of study vaccine and had safety follow-up. Each participant was counted only once within a study Period and only once Overall.

End point type	Secondary

End point timeframe:

Period 1 (up to 14 days after Visit 1 [V1] or V2), Period 2 (up to 14 days after V3 or V4), Period 3 (up to 14 days after V5 or V6), and Overall (up to 14 days after any visit)

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	96		
Units: Percentage of participants				
number (not applicable)				
Period 1 (up to 14 days after V1 or V2) (n=94, 96)	2.1	4.2		
Period 2 (up to 14 days after V3 or V4) (n=94, 96)	0	8.3		
Period 3 (up to 14 days after V5 or V6) (n=94, 95)	0	2.1		
Overall (up to 14 days after any visit) (n=94, 96)	2.1	10.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers for Diphtheria Toxin Antibody

End point title	Geometric Mean Titers for Diphtheria Toxin Antibody

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

End point type	Secondary

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	93	94		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Baseline	0.025 (0.018 to 0.034)	0.019 (0.014 to 0.026)		
4 to 6 weeks after the third dose of DTP-IPV	2.377 (2.032 to 2.78)	2.493 (2.165 to 2.871)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers for Tetanus Toxin Antibody

End point title	Geometric Mean Titers for Tetanus Toxin Antibody

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

End point type	Secondary

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	93	94		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Baseline	0.082 (0.059 to 0.114)	0.093 (0.067 to 0.128)		
4 to 6 weeks after the third dose of DTP-IPV	1.001 (0.702 to 1.428)	1.338 (1.009 to 1.774)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers for Pertussis Toxin Antibody

End point title	Geometric Mean Titers for Pertussis Toxin Antibody

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

End point type	Secondary

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	93	94		
Units: EU/mL				
geometric mean (confidence interval 95%)				

Baseline	2.67 (2.143 to 3.328)	2.757 (2.278 to 3.338)		
4 to 6 weeks after the third dose of DTP-IPV	198.811 (177.43 to 222.768)	241.857 (218.225 to 268.049)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers for Pertussis FHA Antibody

End point title	Geometric Mean Titers for Pertussis FHA Antibody

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

End point type	Secondary

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	93[8]	94		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Baseline	7.513 (6.285 to 8.98)	6.951 (5.703 to 8.472)		
4 to 6 weeks after the third dose of DTP-IPV	77.386 (67.959 to 88.119)	88.275 (76.065 to 102.445)		

Notes:

[8] - 6.951

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers for Poliovirus Type 1 Antibody

End point title	Geometric Mean Titers for Poliovirus Type 1 Antibody

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. Poliovirus antibodies are expressed as neutralising antibody (NA) titers. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

End point type	Secondary

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	93	94		
Units: NA titer				
geometric mean (confidence interval 95%)				
Baseline	23.5 (17.21 to 32.05)	21.1 (15.47 to 28.76)		
4 to 6 weeks after the third dose of DTP-IPV	1578 (1237.3 to 2012)	1703 (1314.4 to 2207)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers for Poliovirus Type 2 Antibody

End point title	Geometric Mean Titers for Poliovirus Type 2 Antibody

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. Poliovirus antibodies are expressed as neutralising antibody (NA) titers. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

End point type	Secondary

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	93	94		
Units: NA titer				
geometric mean (confidence interval 95%)				
Baseline	32 (23.97 to 42.72)	27.8 (20.64 to 37.49)		
4 to 6 weeks after the third dose of DTP-IPV	2886 (2346.9 to 3547.8)	3259 (2678.2 to 3965.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers for Poliovirus Type 3 Antibody

End point title	Geometric Mean Titers for Poliovirus Type 3 Antibody

End point description:

Participant serum was collected for determination of antibody responses before the first dose of study vaccine (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV. Poliovirus antibodies are expressed as neutralising (NA) titers. The per-protocol population included participants who received the 3 scheduled doses of DTP-IPV according to guidelines and did not have an important protocol deviation that may substantially affect the results of the endpoint.

End point type	Secondary

End point timeframe:

Predose (Baseline) and 4 to 6 weeks after the third dose of DTP-IPV

End point values	Concomitant RotaTeqTM + DTP-IPV	Staggered RotaTeqTM + DTP-IPV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	93	94		
Units: NA titer				
geometric mean (confidence interval 95%)				
Baseline	3.9 (3.43 to 4.43)	4.8 (3.92 to 5.85)		
4 to 6 weeks after the third dose of DTP-IPV	2377 (1973.1 to 2864)	2671 (2193.5 to 3251.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events: up to 14 days after any study visit; all deaths, vaccine-related serious adverse events, overdoses, and intussusception: up to 26 weeks after Visit 1

Adverse event reporting additional description:

The safety population included randomised participants who received >=1 dose of study vaccine and had safety follow-up.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Staggered RotaTeqTM + DTP-IPV

Reporting group description:

RotaTeqTM (2 mL oral dose) administered at Visit 1 (Day 1), Visit 3 (6-8 weeks after Visit 1), and Visit 5 (6-8 weeks after Visit 3) and DTP-IPV (0.5 mL subcutaneous injection) administered at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

Reporting group title	Concomitant RotaTeqTM + DTP-IPV

Reporting group description:

RotaTeqTM (2 mL oral dose) and DTP-IPV (0.5 mL subcutaneous injection) administered concomitantly at Visit 2 (>=4 weeks after Visit 1), Visit 4 (6-8 weeks after Visit 2), and Visit 6 (6-8 weeks after Visit 4)

Serious adverse events	Staggered RotaTeqTM + DTP-IPV	Concomitant RotaTeqTM + DTP-IPV	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 96 (2.08%)	0 / 94 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 96 (1.04%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 96 (1.04%)	0 / 94 (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	Staggered RotaTeqTM + DTP-IPV	Concomitant RotaTeqTM + DTP-IPV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 96 (82.29%)	57 / 94 (60.64%)	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	5 / 96 (5.21%)	2 / 94 (2.13%)	
occurrences (all)	7	2	
Pyrexia			
subjects affected / exposed	22 / 96 (22.92%)	10 / 94 (10.64%)	
occurrences (all)	27	10	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	45 / 96 (46.88%)	24 / 94 (25.53%)	
occurrences (all)	86	41	
Infantile spitting up			
subjects affected / exposed	6 / 96 (6.25%)	0 / 94 (0.00%)	
occurrences (all)	7	0	
Vomiting			
subjects affected / exposed	16 / 96 (16.67%)	8 / 94 (8.51%)	
occurrences (all)	23	15	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	7 / 96 (7.29%)	7 / 94 (7.45%)	
occurrences (all)	8	8	
Upper respiratory tract inflammation			
subjects affected / exposed	12 / 96 (12.50%)	9 / 94 (9.57%)	
occurrences (all)	18	10	
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	9 / 96 (9.38%)	6 / 94 (6.38%)	
occurrences (all)	9	6	
Eczema infantile			

subjects affected / exposed	7 / 96 (7.29%)	7 / 94 (7.45%)	
occurrences (all)	7	7	
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 96 (4.17%)	5 / 94 (5.32%)	
occurrences (all)	5	5	
Conjunctivitis			
subjects affected / exposed	6 / 96 (6.25%)	2 / 94 (2.13%)	
occurrences (all)	6	2	
Nasopharyngitis			
subjects affected / exposed	20 / 96 (20.83%)	7 / 94 (7.45%)	
occurrences (all)	24	7	
Upper respiratory tract infection			
subjects affected / exposed	12 / 96 (12.50%)	9 / 94 (9.57%)	
occurrences (all)	15	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported