

**Clinical trial results:****A Double-Blind, Randomized, Placebo-Controlled, Safety and Tolerability Study of Live Pentavalent Human-Bovine Rotavirus Reassortant Vaccine in Chinese Healthy Adults, Children and Infants
Summary**

EudraCT number	2017-000263-32
Trial protocol	Outside EU/EEA
Global end of trial date	26 March 2010

Results information

Result version number	v1 (current)
This version publication date	18 May 2017
First version publication date	18 May 2017

Trial information**Trial identification**

Sponsor protocol code	V260-028
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00953056
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	26 March 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2010
Global end of trial reached?	Yes
Global end of trial date	26 March 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study assessed the safety and tolerability of RotaTeq™ (V260) in the healthy Chinese populations.

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. The following additional measure defined for this individual study was in place for the protection of trial participants: the primary investigator and the Ethics Review Committee reviewed blinded safety data and decided to move forward to the next cohort (Cohort I, then II, then III) based on their best clinical judgment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 September 2009
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	China: 144
Worldwide total number of subjects	144
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)	48
Children (2-11 years)	48
Adolescents (12-17 years)	0
Adults (18-64 years)	48
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled into 3 cohorts. Randomization ratio was 1:1 (RotaTeq™ (V260):placebo) in each cohort. The study was conducted sequentially: Cohort I followed by Cohort II followed by Cohort III, with the primary investigator and Ethics Review Committee reviewing blinded safety data before the next cohort.

Pre-assignment

Screening details:

Healthy Chinese participants were enrolled in the study.

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	Investigator, Carer, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 Rotateq™

Arm description:

Adults ages 19 - 47 years randomized to receive a single dose of RotaTeq™

Arm type	Experimental
Investigational medicinal product name	Rotateq™
Investigational medicinal product code	
Other name	V260, Rotavirus vaccine, live, oral, pentavalent. The 2-mL vaccine consists of an oral solution of 5 live human-bovine reassortant rotaviruses.
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Single 2.0 mL dose of V260 (RotaTeq™) administered orally at enrollment

Arm title	Cohort I Placebo
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Arm description:

Adults ages 19 - 47 years randomized to receive a single dose of placebo

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:

Single 2.0 mL dose of matching placebo to Rotateq™ administered orally at enrollment

Arm title	Cohort II RotaTeq™
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Arm description:

Children ages 2 - 6 years randomized to receive a single dose of RotaTeq™

Arm type	Experimental
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Investigational medicinal product name	Rotateq™
Investigational medicinal product code	
Other name	V260, Rotavirus vaccine, live, oral, pentavalent. The 2-mL vaccine consists of an oral solution of 5 live human-bovine reassortant rotaviruses.
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details: Single 2.0 mL dose of V260 (RotaTeq™) administered orally at enrollment	
Arm title	Cohort II Placebo
Arm description: Children ages 2 - 6 years randomized to receive a single dose of placebo	
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: Single 2.0 mL dose of matching placebo to Rotateq™ administered orally at enrollment	
Arm title	Cohort III RotaTeq™
Arm description: Infants ages 6 - 12 weeks randomized to receive RotaTeq™ vaccination administered at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.	
Arm type	Experimental
Investigational medicinal product name	Rotateq™
Investigational medicinal product code	
Other name	V260, Rotavirus vaccine, live, oral, pentavalent. The 2-mL vaccine consists of an oral solution of 5 live human-bovine reassortant rotaviruses.
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details: 2.0 mL doses of V260 (RotaTeq™) administered orally at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.	
Arm title	Cohort III Placebo
Arm description: Infants ages 6 - 12 weeks randomized to receive placebo vaccination administered at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.	
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: 2.0 mL doses of matching placebo to Rotateq™ administered orally at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.	

Number of subjects in period 1	Cohort 1 Rotateq™	Cohort I Placebo	Cohort II RotaTeq™
Started	24	24	24
Completed	24	24	24
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Serious Adverse Event	-	-	-

Number of subjects in period 1	Cohort II Placebo	Cohort III RotaTeq™	Cohort III Placebo
Started	24	24	24
Completed	24	22	20
Not completed	0	2	4
Consent withdrawn by subject	-	2	3
Serious Adverse Event	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1 Rotateq™
Reporting group description: Adults ages 19 - 47 years randomized to receive a single dose of RotaTeq™	
Reporting group title	Cohort I Placebo
Reporting group description: Adults ages 19 - 47 years randomized to receive a single dose of placebo	
Reporting group title	Cohort II RotaTeq™
Reporting group description: Children ages 2 - 6 years randomized to receive a single dose of RotaTeq™	
Reporting group title	Cohort II Placebo
Reporting group description: Children ages 2 - 6 years randomized to receive a single dose of placebo	
Reporting group title	Cohort III RotaTeq™
Reporting group description: Infants ages 6 - 12 weeks randomized to receive RotaTeq™ vaccination administered at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.	
Reporting group title	Cohort III Placebo
Reporting group description: Infants ages 6 - 12 weeks randomized to receive placebo vaccination administered at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.	

Reporting group values	Cohort 1 Rotateq™	Cohort I Placebo	Cohort II RotaTeq™
Number of subjects	24	24	24
Age Categorical Units: Subjects			
6 weeks to 12 weeks (infants)	0	0	0
2 years to 6 years (children)	0	0	24
19 years to 47 years (adults)	24	24	0
Age Continuous Units: years			
arithmetic mean	37.8	36	3.6
standard deviation	± 8	± 7.6	± 1.1
Gender Categorical Units: Subjects			
Female	13	17	10
Male	11	7	14
Region of Enrollment Units: Subjects			
China	24	24	24

Reporting group values	Cohort II Placebo	Cohort III RotaTeq™	Cohort III Placebo
Number of subjects	24	24	24
Age Categorical Units: Subjects			
6 weeks to 12 weeks (infants)	0	24	24
2 years to 6 years (children)	24	0	0

19 years to 47 years (adults)	0	0	0
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Age Continuous Units: years arithmetic mean standard deviation	3.5 ± 1.2	0.169 ± 0.027	0.179 ± 0.029
Gender Categorical Units: Subjects			
Female	11	8	11
Male	13	16	13
Region of Enrollment Units: Subjects			
China	24	24	24

Reporting group values	Total		
Number of subjects	144		
Age Categorical Units: Subjects			
6 weeks to 12 weeks (infants)	48		
2 years to 6 years (children)	48		
19 years to 47 years (adults)	48		
Age Continuous Units: years arithmetic mean standard deviation	-		
Gender Categorical Units: Subjects			
Female	70		
Male	74		
Region of Enrollment Units: Subjects			
China	144		

End points

End points reporting groups

Reporting group title	Cohort 1 Rotateq™
Reporting group description:	Adults ages 19 - 47 years randomized to receive a single dose of RotaTeq™
Reporting group title	Cohort I Placebo
Reporting group description:	Adults ages 19 - 47 years randomized to receive a single dose of placebo
Reporting group title	Cohort II RotaTeq™
Reporting group description:	Children ages 2 - 6 years randomized to receive a single dose of RotaTeq™
Reporting group title	Cohort II Placebo
Reporting group description:	Children ages 2 - 6 years randomized to receive a single dose of placebo
Reporting group title	Cohort III RotaTeq™
Reporting group description:	Infants ages 6 - 12 weeks randomized to receive RotaTeq™ vaccination administered at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.
Reporting group title	Cohort III Placebo
Reporting group description:	Infants ages 6 - 12 weeks randomized to receive placebo vaccination administered at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.

Primary: Number of Participants with a Serious Adverse Event

End point title	Number of Participants with a Serious Adverse Event ^[1]
End point description:	An adverse event (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the sponsor's product, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the sponsor's product, is also an AE. A serious AE is an AE that results in death, is life threatening, results in or prolongs a hospitalization, is a congenital anomaly or birth defect, is a cancer, is an overdose, or may jeopardize the participant and require medical or surgical intervention. The population analyzed included all participants who received at least one dose of study drug and had safety follow-up.
End point type	Primary
End point timeframe:	Up to 14 days post vaccination
Notes:	[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analysis was planned or conducted for this endpoint

End point values	Cohort 1 Rotateq™	Cohort I Placebo	Cohort II RotaTeq™	Cohort II Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	24	24	24
Units: Participants	0	0	0	0

End point values	Cohort III RotaTeq™	Cohort III Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Participants	0	3		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Serious Adverse Events

End point title	Number of Serious Adverse Events ^[2]
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End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the sponsor's product, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the sponsor's product, is also an AE. A serious AE is an AE that results in death, is life threatening, results in or prolongs a hospitalization, is a congenital anomaly or birth defect, is a cancer, is an overdose, or may jeopardize the participant and require medical or surgical intervention. The population analyzed included all participants who received at least one dose of study drug and had safety follow-up.

End point type	Primary
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End point timeframe:

Up to 14 days post vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was planned or conducted for this endpoint

End point values	Cohort 1 Rotateq™	Cohort I Placebo	Cohort II RotaTeq™	Cohort II Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	24	24	24
Units: Events	0	0	0	0

End point values	Cohort III RotaTeq™	Cohort III Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Events	0	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Infants with Fecal Vaccine Virus Shedding

End point title	Number of Infants with Fecal Vaccine Virus Shedding ^[3]
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End point description:

Fecal shedding of vaccine rotavirus in Cohort III (infants) was evaluated by determining the number of participants whose stool was positive by both (1) the Enzyme-linked Immunosorbent Assay (EIA) to detect the rotavirus antigen, and (2) PCR VP6 Genotyping (a polymerase chain reaction assay specific for rotavirus genome 6, coding for the VP6 protein of the vaccine virus). For analysis, two stool samples were collected per participant on separate days between Day 3 and Day 7 following each vaccination dose. The population analyzed included participants in Cohort III who received the scheduled dose of vaccination and for whom the stool samples were available for testing. This endpoint applied to Cohort III only.

End point type	Secondary
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End point timeframe:

Between Day 3 and Day 7 following each of 3 doses

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: This endpoint applied to Cohort III only

End point values	Cohort III RotaTeq™	Cohort III Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Participants				
Postdose 1 (n=23, 24)	3	0		
Postdose 2 (n=21, 22)	2	0		
Postdose 3 (n=22, 20)	3	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Cohorts I and II: up to 14 days after vaccination; Cohort III: up to 14 days after any of three vaccinations

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Cohort 1 Rotateq™
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Reporting group description:

Adults ages 19 - 47 years randomized to receive a single dose of RotaTeq™

Reporting group title	Cohort I Placebo
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Reporting group description:

Adults ages 19 - 47 years randomized to receive a single dose of placebo

Reporting group title	Cohort II RotaTeq™
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Reporting group description:

Children ages 2 - 6 years randomized to receive a single dose of RotaTeq™

Reporting group title	Cohort II Placebo
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Reporting group description:

Children ages 2 - 6 years randomized to receive a single dose of placebo

Reporting group title	Cohort III RotaTeq™
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Reporting group description:

Infants ages 6 - 12 weeks randomized to receive RotaTeq™ vaccination administered at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.

Reporting group title	Cohort III Placebo
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Reporting group description:

Infants ages 6 - 12 weeks randomized to receive placebo vaccination administered at 3 separate visits scheduled 28 to 70 days apart. The third dose was administered by 32 weeks of age.

Serious adverse events	Cohort 1 Rotateq™	Cohort I Placebo	Cohort II RotaTeq™
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (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			
Bronchopneumonia			

subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (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
Encephalitis viral			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (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	Cohort II Placebo	Cohort III RotaTeq™	Cohort III Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	3 / 24 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Cohort 1 Rotateq™	Cohort I Placebo	Cohort II RotaTeq™
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 24 (25.00%)	2 / 24 (8.33%)	6 / 24 (25.00%)
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 3	1 / 24 (4.17%) 1	0 / 24 (0.00%) 0
General disorders and administration site conditions Malaise subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	0 / 24 (0.00%) 0	0 / 24 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	1 / 24 (4.17%) 1	4 / 24 (16.67%) 4
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	0 / 24 (0.00%) 0	1 / 24 (4.17%) 1
Vomiting subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	0 / 24 (0.00%) 0	1 / 24 (4.17%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	0 / 24 (0.00%) 0	0 / 24 (0.00%) 0
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	0 / 24 (0.00%) 0	1 / 24 (4.17%) 1

Non-serious adverse events	Cohort II Placebo	Cohort III RotaTeq™	Cohort III Placebo
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 24 (12.50%)	18 / 24 (75.00%)	14 / 24 (58.33%)
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	0 / 24 (0.00%) 0	0 / 24 (0.00%) 0
General disorders and administration site conditions Malaise subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	0 / 24 (0.00%) 0	0 / 24 (0.00%) 0

Pyrexia subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	9 / 24 (37.50%) 11	5 / 24 (20.83%) 8
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 2	13 / 24 (54.17%) 23	8 / 24 (33.33%) 19
Vomiting subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	9 / 24 (37.50%) 22	12 / 24 (50.00%) 25
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 24 (4.17%) 1	2 / 24 (8.33%) 2
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 24 (4.17%) 1	2 / 24 (8.33%) 3	2 / 24 (8.33%) 4

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