Clinical trial results:
A Double-Blind, Randomized, Controlled, Multicenter Study to Evaluate the Safety, Tolerability, and Immunogenicity of a New Formulation of RotaTeq™

Summary

EudraCT number	2012-001611-23
Trial protocol	ES SE FI CZ PL DK
Global end of trial date	25 March 2014

Results information

Result version number	v2 (current)
This version publication date	01 July 2020
First version publication date	13 June 2015
Version creation reason	• Correction of full data set updating/correcting to indicate Art 46 applicable study

Trial information

Trial identification

Sponsor protocol code	V260-035

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01600092
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	25 March 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 March 2014
Global end of trial reached?	Yes
Global end of trial date	25 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A study to compare safety, tolerability, and immunogenicity of a new formulation of RotaTeq™ with the existing formulation in infants. The primary hypothesis of the study is that the new formulation will be noninferior to the existing formulation on the basis of immunogenicity.

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	29 April 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	Spain: 118
Country: Number of subjects enrolled	Sweden: 57
Country: Number of subjects enrolled	United States: 237
Country: Number of subjects enrolled	Canada: 103
Country: Number of subjects enrolled	Czech Republic: 78
Country: Number of subjects enrolled	Denmark: 49
Country: Number of subjects enrolled	Finland: 138
Country: Number of subjects enrolled	Israel: 80
Country: Number of subjects enrolled	Mexico: 73
Country: Number of subjects enrolled	Poland: 87
Worldwide total number of subjects	1020
EEA total number of subjects	527

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)	1020
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 1039 participants were screened

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, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	RotaTeq™ Experimental Formulation

Arm description:

Three 2.0 mL oral doses of RotaTeq™ experimental formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).

Arm type	Experimental
Investigational medicinal product name	RotaTeq™ Experimental Formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Three 2.0 mL oral doses of RotaTeq™ experimental formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).

Arm title	RotaTeq™ Existing Formulation

Arm description:

Three 2.0 mL oral doses of RotaTeq™ existing formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).

Arm type	Active comparator
Investigational medicinal product name	RotaTeq™ Existing Formulation
Investigational medicinal product code	
Other name	V260
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Three 2.0 mL oral doses of RotaTeq™ existing formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).

Number of subjects in period 1	RotaTeq™ Experimental Formulation	RotaTeq™ Existing Formulation
Started	513	507
Received at least 1 vaccination	510	504
Received all 3 vaccinations	500	494
Completed	495	491
Not completed	18	16
Physician decision	1	1
Adverse event, non-fatal	2	-
Randomized but not vaccinated	3	3
Lost to follow-up	4	6
Withdrawal by parent/guardian	8	6

Baseline characteristics

Reporting groups	
Reporting group title	RotaTeq™ Experimental Formulation
Reporting group description:	
Three 2.0 mL oral doses of RotaTeq™ experimental formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).	
Reporting group title	RotaTeq™ Existing Formulation
Reporting group description:	
Three 2.0 mL oral doses of RotaTeq™ existing formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).	

Reporting group values	RotaTeq™ Experimental Formulation	RotaTeq™ Existing Formulation	Total
Number of subjects	513	507	1020
Age categorical			
Units: Subjects			
Age continuous			
Units: weeks			
arithmetic mean	8.4	8.3	
standard deviation	± 1.4	± 1.4	-
Gender categorical			
Units: Subjects			
Female	232	240	472
Male	281	267	548

End points

End points reporting groups

Reporting group title	RotaTeq™ Experimental Formulation
Reporting group description:	
Three 2.0 mL oral doses of RotaTeq™ experimental formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).	
Reporting group title	RotaTeq™ Existing Formulation
Reporting group description:	
Three 2.0 mL oral doses of RotaTeq™ existing formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).	

Primary: Geometric Mean Titer of Serum Neutralizing Antibody Response to Human Rotavirus Serotypes G1, G2, G3, G4, and P1A[8]

End point title	Geometric Mean Titer of Serum Neutralizing Antibody Response to Human Rotavirus Serotypes G1, G2, G3, G4, and P1A[8]
End point description:	
The population included participants who received the 3 scheduled doses of study vaccine, did not have important protocol deviations, and had follow-up results for the endpoint	
End point type	Primary
End point timeframe:	
42 days after vaccination 3 (up to 185 days)	

End point values	RotaTeq™ Experimental Formulation	RotaTeq™ Existing Formulation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	480	482		
Units: Titer				
geometric mean (confidence interval 95%)				
Serotype G1	99.8 (89.7 to 111.1)	106.1 (94.6 to 119)		
Serotype G2	30 (27 to 33.3)	26.3 (23.7 to 29.1)		
Serotype G3	82.8 (74.2 to 92.5)	25.2 (22.6 to 28.1)		
Serotype G4	78.9 (72.3 to 86.1)	71.5 (65.4 to 78.1)		
Serotype P1A[8]	106.9 (96.5 to 118.4)	90.1 (80.2 to 101.2)		

Statistical analyses

Statistical analysis title	Non-inferiority Serotype G1

Statistical analysis description:

GMTs and GMT ratio were based on a model with terms for treatment and country, with the constraint that the mean baseline value is the same for both treatment groups. Non-inferiority required that the lower bound of the 2-sided 95% confidence interval of the GMT ratio is >0.67. Since the model used all available data at both baseline and postvaccination, the number of participants included in the analysis was 983 (962 participants had postvaccination data).

Comparison groups	RotaTeq™ Experimental Formulation v RotaTeq™ Existing Formulation
Number of subjects included in analysis	962
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio (Experimental/Existing)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.07

Statistical analysis title	Non-inferiority Serotype G2

Statistical analysis description:

GMTs and GMT ratio were based on a model with terms for treatment and country, with the constraint that the mean baseline value is the same for both treatment groups. Non-inferiority required that the lower bound of the 2-sided 95% confidence interval of the GMT ratio is >0.67. Since the model used all available data at both baseline and postvaccination, the number of participants included in the analysis was 983 (962 participants had postvaccination data).

Comparison groups	RotaTeq™ Experimental Formulation v RotaTeq™ Existing Formulation
Number of subjects included in analysis	962
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio (Experimental/Existing)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.33

Statistical analysis title	Non-inferiority Serotype G3

Statistical analysis description:

GMTs and GMT ratio were based on a model with terms for treatment and country, with the constraint that the mean baseline value is the same for both treatment groups. Non-inferiority required that the lower bound of the 2-sided 95% confidence interval of the GMT ratio is >0.67. Since the model used all available data at both baseline and postvaccination, the number of participants included in the analysis was 983 (962 participants had postvaccination data).

Comparison groups	RotaTeq™ Experimental Formulation v RotaTeq™ Existing Formulation

Number of subjects included in analysis	962
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio (Experimental/Existing)
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.75
upper limit	3.74

Statistical analysis title	Non-inferiority Serotype G4

Statistical analysis description:

GMTs and GMT ratio were based on a model with terms for treatment and country, with the constraint that the mean baseline value is the same for both treatment groups. Non-inferiority required that the lower bound of the 2-sided 95% confidence interval of the GMT ratio is >0.67. Since the model used all available data at both baseline and postvaccination, the number of participants included in the analysis was 983 (962 participants had postvaccination data).

Comparison groups	RotaTeq™ Experimental Formulation v RotaTeq™ Existing Formulation
Number of subjects included in analysis	962
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio (Experimental/Existing)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.2

Statistical analysis title	Non-inferiority Serotype P1A[8]

Statistical analysis description:

GMTs and GMT ratio were based on a model with terms for treatment and country, with the constraint that the mean baseline value is the same for both treatment groups. Non-inferiority required that the lower bound of the 2-sided 95% confidence interval of the GMT ratio is >0.67. Since the model used all available data at both baseline and postvaccination, the number of participants included in the analysis was 983 (962 participants had postvaccination data).

Comparison groups	RotaTeq™ Experimental Formulation v RotaTeq™ Existing Formulation
Number of subjects included in analysis	962
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMT Ratio (Experimental/Existing)
Point estimate	1.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.35

Secondary: Number of Participants With Tier-1 Adverse Events: Diarrhea, Vomiting, Elevated Temperature, and Irritability

End point title	Number of Participants With Tier-1 Adverse Events: Diarrhea, Vomiting, Elevated Temperature, and Irritability

End point description:

The population included participants who received at least one dose of study vaccine. Participants were assigned to treatment groups based on the vaccine received as the first dose.

An adverse event is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, 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 study vaccine is also an adverse event. Protocol-defined Tier-1 adverse events to be collected up to 7 days after any vaccination were diarrhea, vomiting, elevated temperature (rectal >=38.1° C, >=100.5° F), and irritability.

End point type	Secondary

End point timeframe:

Up to 7 days after any vaccination (up to 147 days)

End point values	RotaTeq™ Experimental Formulation	RotaTeq™ Existing Formulation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	509	505		
Units: Participants				
Diarrhea	144	128		
Vomiting	84	92		
Elevated temperature	217	223		
Irritability	58	64		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Tier-1 Adverse Events: Intussusception

End point title	Number of Participants With Tier-1 Adverse Events: Intussusception

End point description:

The population included participants who received at least one dose of study vaccine. Participants were assigned to treatment groups based on the vaccine received as the first dose.

End point type	Secondary

End point timeframe:

Up to Day 185

End point values	RotaTeq™ Experimental Formulation	RotaTeq™ Existing Formulation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	509	505		
Units: Participants	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer of Serum Anti-Rotavirus Immunoglobulin A

End point title	Geometric Mean Titer of Serum Anti-Rotavirus Immunoglobulin A

End point description:

The population included participants who received the 3 scheduled doses of study vaccine, did not have important protocol deviations, and had follow-up results for the endpoint

End point type	Secondary

End point timeframe:

42 days after vaccination 3 (up to 185 days)

End point values	RotaTeq™ Experimental Formulation	RotaTeq™ Existing Formulation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	474	474		
Units: Titer				
geometric mean (confidence interval 95%)	240.5 (210.4 to 274.8)	235.5 (204.1 to 271.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With >=3-fold Rise From Baseline in GMT of Serum Neutralizing Antibody to Human Rotavirus Serotypes G1, G2, G3, G4, and P1A[8]

End point title	Percentage of Participants With >=3-fold Rise From Baseline in GMT of Serum Neutralizing Antibody to Human Rotavirus Serotypes G1, G2, G3, G4, and P1A[8]

End point description:

The population included participants who received the 3 scheduled doses of study vaccine, did not have important protocol deviations, and had baseline and follow-up results for the endpoint.

End point type	Secondary

End point timeframe:

Baseline and 42 days after vaccination 3 (up to 185 days)

End point values	RotaTeq™ Experimental Formulation	RotaTeq™ Existing Formulation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	480	481		
Units: Percentage of participants				
number (confidence interval 95%)				
Serotype G1	56 (51.5 to 60.5)	53.8 (49.3 to 58.4)		
Serotype G2	30.4 (26.3 to 34.7)	26.8 (22.9 to 31)		
Serotype G3	65.8 (61.4 to 70.1)	33.3 (29.1 to 37.7)		
Serotype G4	58.3 (53.8 to 62.8)	49.7 (45.1 to 54.3)		
Serotype P1A[8]	49.6 (45 to 54.2)	42.6 (38.2 to 47.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events: up to 42 days after any vaccination; serious adverse events, deaths, and intussusception: up to Day 185

Adverse event reporting additional description:

The participants at risk includes participants who received at least one dose of study vaccine and had follow-up

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	RotaTeq™ Existing Formulation

Reporting group description:

Three 2.0 mL oral doses of RotaTeq™ existing formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).

Reporting group title	RotaTeq™ Experimental Formulation

Reporting group description:

Three 2.0 mL oral doses of RotaTeq™ experimental formulation. Vaccination 1 was administered between 6 and 12 weeks of age and the third vaccination was administered before 32 weeks of age. Each vaccination was separated from the next by ≥ 4 weeks (28 days).

Serious adverse events	RotaTeq™ Existing Formulation	RotaTeq™ Experimental Formulation	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 499 (2.40%)	20 / 508 (3.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 499 (0.20%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous haematoma			
subjects affected / exposed	1 / 499 (0.20%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hypersomnia			

subjects affected / exposed	0 / 499 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 499 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 499 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intussusception			
subjects affected / exposed	0 / 499 (0.00%)	2 / 508 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 499 (0.20%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Restlessness			
subjects affected / exposed	1 / 499 (0.20%)	0 / 508 (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			
Anal abscess			
subjects affected / exposed	1 / 499 (0.20%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			

subjects affected / exposed	1 / 499 (0.20%)	3 / 508 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 499 (0.20%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 499 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 499 (0.20%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 499 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae virus infection			
subjects affected / exposed	0 / 499 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 499 (0.00%)	2 / 508 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 499 (0.20%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	1 / 499 (0.20%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 499 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 499 (0.20%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 499 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 499 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 499 (0.20%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 499 (0.20%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	RotaTeq™ Existing Formulation	RotaTeq™ Experimental Formulation	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	385 / 499 (77.15%)	398 / 508 (78.35%)	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	152 / 499 (30.46%)	151 / 508 (29.72%)	
occurrences (all)	231	211	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	22 / 499 (4.41%)	30 / 508 (5.91%)	
occurrences (all)	29	33	
Diarrhoea			
subjects affected / exposed	156 / 499 (31.26%)	173 / 508 (34.06%)	
occurrences (all)	276	307	
Vomiting			
subjects affected / exposed	107 / 499 (21.44%)	102 / 508 (20.08%)	
occurrences (all)	180	175	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	44 / 499 (8.82%)	36 / 508 (7.09%)	
occurrences (all)	50	39	
Psychiatric disorders			
Irritability			
subjects affected / exposed	77 / 499 (15.43%)	65 / 508 (12.80%)	
occurrences (all)	113	98	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	25 / 499 (5.01%)	27 / 508 (5.31%)	
occurrences (all)	25	35	
Nasopharyngitis			
subjects affected / exposed	83 / 499 (16.63%)	79 / 508 (15.55%)	
occurrences (all)	113	106	
Otitis media			
subjects affected / exposed	29 / 499 (5.81%)	20 / 508 (3.94%)	
occurrences (all)	33	26	
Rhinitis			

subjects affected / exposed	40 / 499 (8.02%)	42 / 508 (8.27%)	
occurrences (all)	56	53	
Upper respiratory tract infection			
subjects affected / exposed	67 / 499 (13.43%)	78 / 508 (15.35%)	
occurrences (all)	87	97	

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