Clinical trial results:
An open-label, randomised, comparative, multi-centre study of the immunogenicity and safety of the concomitant use of a live pentavalent rotavirus vaccine (RotaTeq®) and a meningococcal group C conjugate (MCC) vaccine in healthy infants

Summary

EudraCT number	2006-005445-11
Trial protocol	FI
Global end of trial date	23 October 2007

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	22 July 2015

Trial information

Trial identification

Sponsor protocol code	S06-ROT-304

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00443846
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur MSD S.N.C.
Sponsor organisation address	162 avenue Jean Jaurès - CS 50712, Lyon Cedex 07, France, 69367
Public contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C., ClinicalTrialsDisclosure@spmsd.com
Scientific contact	Clinical Trials Disclosure, Sanofi Pasteur MSD S.N.C., ClinicalTrialsDisclosure@spmsd.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	23 October 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 October 2007
Global end of trial reached?	Yes
Global end of trial date	23 October 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that RotaTeq® can be administered concomitantly with MCC vaccine to healthy infants without impairing the antibody seroprotection rate to meningococcal Group C serotype as measured by serum bactericidal antibody with rabbit complement (rSBA) at 28 days following the last dose.

Protection of trial subjects:

Healthy subjects with hypersensitivity to any component of RotaTeq® (e.g. sucrose) or of NeisVac-C® (MCC vaccine) (including tetanus toxoid) were not included.
Vaccines were administered by qualified study personnel.
After each vaccination, subjects were kept under observation for at least 20 minutes to ensure their safety.

Background therapy: -

Evidence for comparator:

The primary objective of the study was to demonstrate that RotaTeq can be administered concomitantly with MCC vaccine without impairing the antibody responses to MCC vaccine in order to support the use of RotaTeq in countries in which MCC vaccine is administered routinely to infants. Thus, the study design allowed the assessment of concomitant versus sequential administration of RotaTeq and MCC vaccine when the MCC vaccine was given at the same age in both groups.

Actual start date of recruitment	13 February 2007
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	Finland: 247
Worldwide total number of subjects	247
EEA total number of subjects	247

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)	247
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:

Study subjects were enrolled between 13 February 2007 and 4 April 2007 in 9 active centres in Finland.

Pre-assignment

Screening details:

249 subjects were screened.
247 subjects were randomised.
239 subjects were vaccinated.
230 subjects completed the study.

Period 1

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

Blinding implementation details:

Not applicable as this study was open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Concomitant administration

Arm description:

Subjects received the 2 study vaccines concomitantly:
3 doses of RotaTeq (pentavalent combination live vaccine of 5 human-bovine reassortant rotavirus strains) by oral route: dose 1 at 10-11 weeks of age, dose 2 at 20-21 weeks of age, and dose 3 at 24-25 weeks of age
2 doses of MCC vaccine (NeisVac-C = Meningococcal group C polysaccharide Conjugate vaccine adsorbed) by intramuscular route: dose 1 at 10-11 weeks of age, and dose 2 at 20-21 weeks of age.
Subjects were blood sampled (i) before vaccination = pre-vaccination, (ii) 28 to 42 days following dose 2 of MCC vaccine = post-MCC vaccination, and (iii) 42 days ±3 days following dose 3 of RotaTeq = post-RotaTeq vaccination.
Note: Routine pentavalent vaccine against diphtheria, tetanus, pertussis, poliomyelitis and Haemophilus influenzae infections was preferably to be given at 10-11 and 20-21 weeks of age.

Arm type	Experimental
Investigational medicinal product name	RotaTeq®
Investigational medicinal product code	RotaTeq
Other name	
Pharmaceutical forms	Oral solution in single-dose container
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral route, 3 doses: dose 1 at 10-11 weeks of age, dose 2 at 20-21 weeks of age, and dose 3 at 24-25 weeks of age.

Investigational medicinal product name	NeisVac-C®
Investigational medicinal product code	MCC
Other name	MCC vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route (preferably anterolateral region of the thigh), 2 doses: dose 1 at 10-11 weeks of age, and dose 2 at 20-21 weeks of age.

Arm title	Sequential administration

Arm description:

Subjects received the 2 study vaccines sequentially:

3 doses of RotaTeq (pentavalent combination live vaccine of 5 human-bovine reassortant rotavirus strains) by oral route: dose 1 at 6-7 weeks of age, dose 2 at 15-16 weeks of age, and dose 3 at 24-25 weeks of age,
2 doses of MCC vaccine (NeisVac-C = Meningococcal group C polysaccharide Conjugate vaccine adsorbed) by intramuscular route: dose 1 at 10-11 weeks of age, and dose 2 at 20-21 weeks of age.
Subjects were blood sampled (i) before any vaccination = pre-vaccination, (ii) 28 to 42 days following dose 2 of MCC vaccine = post-MCC vaccination, and (iii) 42 days ±3 days following dose 3 of RotaTeq = post-RotaTeq vaccination.
Note: Routine pentavalent vaccine against diphtheria, tetanus, pertussis, poliomyelitis and Haemophilus influenzae infections was preferably to be given at 10-11 and 20-21 weeks of age.

Arm type	Active comparator
Investigational medicinal product name	RotaTeq®
Investigational medicinal product code	RotaTeq
Other name	
Pharmaceutical forms	Oral solution in single-dose container
Routes of administration	Oral use

Dosage and administration details:

2 mL, oral route, 3 doses: dose 1 at 6-7 weeks of age, dose 2 at 15-16 weeks of age, and dose 3 at 24-25 weeks of age.

Investigational medicinal product name	NeisVac-C®
Investigational medicinal product code	MCC
Other name	MCC vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular route (preferably anterolateral region of the thigh), 2 doses: dose 1 at 10-11 weeks of age, and dose 2 at 20-21 weeks of age.

Number of subjects in period 1	Concomitant administration	Sequential administration
Started	124	123
Completed	113	117
Not completed	11	6
Adverse event, non-fatal	1	1
Personal reason	8	3
Subject not vaccinated, no blood sample drawn	1	-
Lost to follow-up	1	2

Baseline characteristics

Reporting groups

Reporting group title	Concomitant administration

Reporting group description:

Subjects received the 2 study vaccines concomitantly:
3 doses of RotaTeq (pentavalent combination live vaccine of 5 human-bovine reassortant rotavirus strains) by oral route: dose 1 at 10-11 weeks of age, dose 2 at 20-21 weeks of age, and dose 3 at 24-25 weeks of age
2 doses of MCC vaccine (NeisVac-C = Meningococcal group C polysaccharide Conjugate vaccine adsorbed) by intramuscular route: dose 1 at 10-11 weeks of age, and dose 2 at 20-21 weeks of age.
Subjects were blood sampled (i) before vaccination = pre-vaccination, (ii) 28 to 42 days following dose 2 of MCC vaccine = post-MCC vaccination, and (iii) 42 days ±3 days following dose 3 of RotaTeq = post-RotaTeq vaccination.
Note: Routine pentavalent vaccine against diphtheria, tetanus, pertussis, poliomyelitis and Haemophilus influenzae infections was preferably to be given at 10-11 and 20-21 weeks of age.

Reporting group title	Sequential administration

Reporting group description:

Subjects received the 2 study vaccines sequentially:
3 doses of RotaTeq (pentavalent combination live vaccine of 5 human-bovine reassortant rotavirus strains) by oral route: dose 1 at 6-7 weeks of age, dose 2 at 15-16 weeks of age, and dose 3 at 24-25 weeks of age,
2 doses of MCC vaccine (NeisVac-C = Meningococcal group C polysaccharide Conjugate vaccine adsorbed) by intramuscular route: dose 1 at 10-11 weeks of age, and dose 2 at 20-21 weeks of age.
Subjects were blood sampled (i) before any vaccination = pre-vaccination, (ii) 28 to 42 days following dose 2 of MCC vaccine = post-MCC vaccination, and (iii) 42 days ±3 days following dose 3 of RotaTeq = post-RotaTeq vaccination.
Note: Routine pentavalent vaccine against diphtheria, tetanus, pertussis, poliomyelitis and Haemophilus influenzae infections was preferably to be given at 10-11 and 20-21 weeks of age.

Reporting group values	Concomitant administration	Sequential administration	Total
Number of subjects	124	123	247
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	124	123	247
Age continuous			
Age in weeks at randomisation visit.			
Units: weeks			
arithmetic mean	7.1	7.2	
standard deviation	± 0.5	± 0.6	-
Gender categorical Units: Subjects			
Female	50	55	105
Male	74	68	142

End points

End points reporting groups

Reporting group title	Concomitant administration

Reporting group description:

Subjects received the 2 study vaccines concomitantly:
3 doses of RotaTeq (pentavalent combination live vaccine of 5 human-bovine reassortant rotavirus strains) by oral route: dose 1 at 10-11 weeks of age, dose 2 at 20-21 weeks of age, and dose 3 at 24-25 weeks of age
2 doses of MCC vaccine (NeisVac-C = Meningococcal group C polysaccharide Conjugate vaccine adsorbed) by intramuscular route: dose 1 at 10-11 weeks of age, and dose 2 at 20-21 weeks of age.
Subjects were blood sampled (i) before vaccination = pre-vaccination, (ii) 28 to 42 days following dose 2 of MCC vaccine = post-MCC vaccination, and (iii) 42 days ±3 days following dose 3 of RotaTeq = post-RotaTeq vaccination.
Note: Routine pentavalent vaccine against diphtheria, tetanus, pertussis, poliomyelitis and Haemophilus influenzae infections was preferably to be given at 10-11 and 20-21 weeks of age.

Reporting group title	Sequential administration

Reporting group description:

Subjects received the 2 study vaccines sequentially:
3 doses of RotaTeq (pentavalent combination live vaccine of 5 human-bovine reassortant rotavirus strains) by oral route: dose 1 at 6-7 weeks of age, dose 2 at 15-16 weeks of age, and dose 3 at 24-25 weeks of age,
2 doses of MCC vaccine (NeisVac-C = Meningococcal group C polysaccharide Conjugate vaccine adsorbed) by intramuscular route: dose 1 at 10-11 weeks of age, and dose 2 at 20-21 weeks of age.
Subjects were blood sampled (i) before any vaccination = pre-vaccination, (ii) 28 to 42 days following dose 2 of MCC vaccine = post-MCC vaccination, and (iii) 42 days ±3 days following dose 3 of RotaTeq = post-RotaTeq vaccination.
Note: Routine pentavalent vaccine against diphtheria, tetanus, pertussis, poliomyelitis and Haemophilus influenzae infections was preferably to be given at 10-11 and 20-21 weeks of age.

Subject analysis set title	Concomitant administration - visit 2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who concomitantly received RotaTeq + MCC vaccine doses 1 at 10-11 weeks of age (visit 2) and who had safety follow-up data at visit 2.

Subject analysis set title	Sequential administration - visit 2
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who received MCC vaccine dose 1 at 10-11 weeks of age (visit 2) and who had safety follow-up data at visit 2.

Subject analysis set title	Concomitant administration - visit 4
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who concomitantly received RotaTeq + MCC vaccine doses 2 at 20-21 weeks of age (visit 4) and who had safety follow-up data at visit 4.

Subject analysis set title	Sequential administration - visit 4
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who received MCC vaccine dose 2 at 20-21 weeks of age (visit 4) and who had safety follow-up data at visit 4.

Primary: Seroprotection rate for the meningococcal Group C (Men C) serotype 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq

End point title	Seroprotection rate for the meningococcal Group C (Men C) serotype 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq

End point description:

The immune response to MCC vaccine was measured by serum bactericidal antibody with rabbit complement (rSBA).

Seroprotection rate for the meningococcal Group C (Men C) serotype, defined as Men C-rSBA titre ≥8 (1/dil), was determined 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq.
Analysis was done on the Per Protocol Set for the MCC vaccine immunogenicity evaluation, i.e. all randomised subjects excluding subjects with protocol deviation that might interfere with the immunogenicity evaluation of the MCC vaccine.

End point type	Primary

End point timeframe:

1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq.

End point values	Concomitant administration	Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	106		
Units: Percentage of subjects				
number (confidence interval 95%)				
Men C-rSBA titre ≥8 (1/dil)	100 (96.5 to 100)	100 (96.6 to 100)		

Statistical analyses

Statistical analysis title	Non-inferiority for Men C seroprotection rate

Statistical analysis description:

The estimate of the difference between Group 1 (concomitant administration) & Group 2 (sequential administration) seroprotection rates was calculated with its 2-sided 95% confidence interval (CI). If the lower bound of the 95% CI was greater than the non-inferiority margin, it was concluded that Group 1 seroprotection rate was non-inferior to the Group 2 one.
Statistical analysis was based on the Miettinen & Nurminen method stratified by centre.
Analysis was done on the PPS for MCC vaccine.

Comparison groups	Concomitant administration v Sequential administration
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in percentages of subjects
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	3.7

Notes:

[1] - For Men C: # PPS for MCC vaccine, N=104, 106 (Groups 1 & 2) # Response rate based on Men C-rSBA titre ≥8 (1/dil) # Non-inferiority margin, -10%.

Secondary: Percentage of subjects with anti-Men C antibody (Ab) titres ≥128 (1/dil) before vaccination and 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq

End point title	Percentage of subjects with anti-Men C antibody (Ab) titres ≥128 (1/dil) before vaccination and 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq

End point description:

Subjects were blood sampled before vaccination (pre-MCC vaccination), and 28 to 42 days following MCC vaccine dose 2, administered concomitantly or not with RotaTeq (post-MCC vaccination).
Percentages of subjects with Men C-rSBA titres ≥128 (1/dil) pre- and post-MCC vaccination are presented hereafter.
Analysis was done on the Per Protocol Set for the MCC vaccine immunogenicity evaluation, i.e. all randomised subjects excluding subjects with protocol deviation that might interfere with the immunogenicity evaluation of the MCC vaccine.

End point type	Secondary

End point timeframe:

Pre-MCC vaccination: before administration of any study vaccines.
Post-MCC vaccination: 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq.

End point values	Concomitant administration	Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	106[2]		
Units: Percentage of subjects				
number (confidence interval 95%)				
Pre-MCC vaccination Men C-rSBA ≥128 (1/dil)	1.9 (0.2 to 6.8)	3.8 (1 to 9.5)		
Post-MCC vaccination Men C-rSBA ≥128 (1/dil)	100 (96.5 to 100)	99.1 (94.9 to 100)		

Notes:

[2] - Pre-MCC vaccination: 1 missing data (N=105)

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres (GMT) of anti-Men C antibodies (Ab) pre-MCC vaccination and 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq

End point title	Geometric Mean Titres (GMT) of anti-Men C antibodies (Ab) pre-MCC vaccination and 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq

End point description:

Subjects were blood sampled before vaccination (pre-MCC vaccination), and 28 to 42 days following MCC vaccine dose 2, administered concomitantly or not with RotaTeq (post-MCC vaccination).
Anti-Men C Ab titres expressed in reciprocal dilution units were measured by serum bactericidal antibody with rabbit complement (rSBA) pre- and post-MCC vaccination.
Analysis was done on the Per Protocol Set for the MCC vaccine immunogenicity evaluation, i.e. all randomised subjects excluding subjects with protocol deviation that might interfere with the immunogenicity evaluation of the MCC vaccine.

End point type	Secondary

End point timeframe:

Pre-MCC vaccination: before administration of any study vaccines.
Post-MCC vaccination: 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq.

End point values	Concomitant administration	Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	106[3]		
Units: Titres				
geometric mean (confidence interval 95%)				
Pre-MCC vaccination Men C-rSBA GMT	2.5 (2.1 to 2.9)	2.6 (2.2 to 3.1)		
Post-MCC vaccination Men C-rSBA GMT	1457.8 (1251.5 to 1698.2)	1262.3 (1074.8 to 1482.5)		

Notes:

[3] - Pre-MCC vaccination: 1 missing data (N=105)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with ≥4-fold increase of Men C-rSBA antibody (Ab) titres from pre- to post-MCC vaccination, i.e. 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq

End point title	Percentage of subjects with ≥4-fold increase of Men C-rSBA antibody (Ab) titres from pre- to post-MCC vaccination, i.e. 1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq

End point description:

Subjects were blood sampled before vaccination (pre-MCC vaccination), and 28 to 42 days following dose 2 of MCC vaccine, administered concomitantly or not with RotaTeq (post-MCC vaccination).
Anti-Men C Ab titres were measured by serum bactericidal antibody with rabbit complement (rSBA) pre- and post-MCC vaccination.
Percentages of subjects with ≥4-fold increase of Men C-rSBA Ab titres from pre- to post-MCC vaccination are presented hereafter.
Analysis was done on the Per Protocol Set for the MCC vaccine immunogenicity evaluation, i.e. all randomised subjects excluding subjects with protocol deviation that might interfere with the immunogenicity evaluation of the MCC vaccine.

End point type	Secondary

End point timeframe:

1 month after MCC vaccine dose 2, administered concomitantly or not with RotaTeq.

End point values	Concomitant administration	Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	105		
Units: Percentage of subjects				
number (confidence interval 95%)				
Pre- to post-MCC vaccination ≥4-fold increase	98.1 (93.2 to 99.8)	98.1 (93.3 to 99.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres (GMT) of serum neutralising antibodies (SNA) to rotavirus serotypes G1, G2, G3, G4 & P1A and serum anti-rotavirus IgA 42 ±3 days following RotaTeq dose 3

End point title	Geometric Mean Titres (GMT) of serum neutralising antibodies (SNA) to rotavirus serotypes G1, G2, G3, G4 & P1A and serum anti-rotavirus IgA 42 ±3 days following RotaTeq dose 3

End point description:

SNA titres to rotavirus serotypes G1, G2, G3, G4 & P1A expressed in dilution unit, and # serum anti-rotavirus IgA titres expressed in units/mL were measured 42 ±3 days following RotaTeq dose 3. Analysis was done on the Per Protocol Set for the RotaTeq immunogenicity evaluation, i.e. all randomised subjects excluding subjects with protocol deviation that might interfere with the immunogenicity evaluation of the RotaTeq.

End point type	Secondary

End point timeframe:

42 ±3 days following RotaTeq dose 3.

End point values	Concomitant administration	Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	104		
Units: Titres				
geometric mean (confidence interval 95%)				
Anti-rotavirus G1 GMT (SNA)	187.2 (148.8 to 235.5)	211.4 (168.6 to 264.9)		
Anti-rotavirus G2 GMT (SNA)	41.9 (33.7 to 52.2)	44.3 (35.6 to 55.1)		
Anti-rotavirus G3 GMT (SNA)	24.2 (18.8 to 31.1)	25.5 (19.8 to 32.9)		
Anti-rotavirus G4 GMT (SNA)	64.7 (51.1 to 82)	76.4 (59.8 to 97.5)		
Anti-rotavirus P1A GMT (SNA)	111.2 (88.3 to 140)	124.3 (99.1 to 156)		
Anti-rotavirus IgA GMT	290.6 (215.1 to 392.5)	363.1 (290.3 to 454.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with ≥3-fold increase of SNA titres to rotavirus serotypes G1, G2, G3, G4 & P1A & serum anti-rotavirus IgA titres from pre- to post-RotaTeq vaccination, i.e. 42 days after RotaTeq dose 3

End point title	Percentage of subjects with ≥3-fold increase of SNA titres to rotavirus serotypes G1, G2, G3, G4 & P1A & serum anti-rotavirus IgA titres from pre- to post-RotaTeq vaccination, i.e. 42 days after RotaTeq dose 3

End point description:

Subjects were blood sampled before vaccination (pre-RotaTeq vaccination), and 42 ±3 days following RotaTeq dose 3 (post-RotaTeq vaccination).

Percentages of subjects with ≥3-fold increase of SNA titres to rotavirus serotypes G1, G2, G3, G4 & P1A and serum anti-rotavirus IgA titres from pre- to post-RotaTeq vaccination are presented hereafter.
Analysis was done on the Per Protocol Set for the RotaTeq immunogenicity evaluation, i.e. all randomised subjects excluding subjects with protocol deviation that might interfere with the immunogenicity evaluation of the RotaTeq.

End point type	Secondary

End point timeframe:

42 ±3 days following RotaTeq dose 3.

End point values	Concomitant administration	Sequential administration		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	104		
Units: Percentage of subjects				
number (confidence interval 95%)				
G1 pre- to post-vaccination ≥3-fold increase	57.1 (46.7 to 67.1)	63.5 (53.4 to 72.7)		
G2 pre- to post-vaccination ≥3-fold increase	33.7 (24.4 to 43.9)	38.5 (29.1 to 48.5)		
G3 pre- to post-vaccination ≥3-fold increase	33.7 (24.4 to 43.9)	37.5 (28.2 to 47.5)		
G4 pre- to post-vaccination ≥3-fold increase	44.9 (34.8 to 55.3)	46.2 (36.3 to 56.2)		
P1A pre- to post-vaccination ≥3-fold increase	32.7 (23.5 to 42.9)	40.4 (30.9 to 50.5)		
IgA pre- to post-vaccination ≥3-fold increase	96.9 (91.3 to 99.4)	98.1 (93.2 to 99.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Global summary of safety from D0 to D13 following visit 2 and visit 4

End point title	Global summary of safety from D0 to D13 following visit 2 and visit 4

End point description:

Adverse events (AEs) occurring following visit 2 (concomitant administration: RotaTeq + MCC vaccine doses 1; sequential administration: MCC vaccine dose 1 alone) & visit 4 (concomitant administration: RotaTeq + MCC vaccine doses 2; sequential administration: MCC vaccine dose 2 alone) were recorded as follows:
From D0 to D6: unsolicited MCC injection-site and solicited daily systemic (diarrhoea, vomiting & pyrexia: rectal temperature ≥38.1°C or fever without temperature measurement) AEs,
From D0 to D13: unsolicited systemic AEs.
AEs at injection sites were always considered as related to MCC vaccine (ISRs). The investigator had to assess whether systemic AEs were vaccine-related systemic AEs or not.
Analysis was done on the Safety Set at visit 2 (N=238) & Safety Set at visit 4 (N=235), i.e. all subjects who received at least 1 dose of the study vaccines and who had safety follow-up data at visits 2 or 4.
Note: "0" means "not applicable".

End point type	Secondary

End point timeframe:

Visit 2: from D0 to D13 following visit 2 (concomitant: RotaTeq + MCC vaccine doses 1; sequential: MCC vaccine dose 1 alone).
Visit 4: from D0 to D13 following visit 4 (concomitant: RotaTeq + MCC vaccine doses 2; sequential: MCC vaccine dose 2 alone).

End point values	Concomitant administration - visit 2	Sequential administration - visit 2	Concomitant administration - visit 4	Sequential administration - visit 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	116	122	115	120
Units: Percentage of subjects				
number (confidence interval 95%)				
At least 1 AE (ISR or systemic AE) (D0-D13)	78.4 (69.9 to 85.5)	65.6 (56.4 to 73.9)	60 (50.4 to 69)	57.5 (48.1 to 66.5)
At least 1 RotaTeq-related AE (D0-D13)	65.5 (56.1 to 74.1)	0 (0 to 0)	42.6 (33.4 to 52.2)	0 (0 to 0)
At least 1 MCC-related AE (D0-D13)	63.8 (54.4 to 72.5)	54.9 (45.7 to 63.9)	49.6 (40.1 to 59)	54.2 (44.8 to 63.3)
At least 1 MCC ISR (D0-D6)	13.8 (8.1 to 21.4)	8.2 (4 to 14.6)	24.3 (16.8 to 33.2)	21.7 (14.7 to 30.1)
At least 1 systemic AE (D0-D13)	75 (66.1 to 82.6)	62.3 (53.1 to 70.9)	53 (43.5 to 62.4)	48.3 (39.1 to 57.6)
At least 1 RotaTeq-related systemic AE (D0-D13)	65.5 (56.1 to 74.1)	0 (0 to 0)	42.6 (33.4 to 52.2)	0 (0 to 0)
At least 1 MCC-related systemic AE (D0-D13)	58.6 (49.1 to 67.7)	50.8 (41.6 to 60)	39.1 (30.2 to 48.7)	42.5 (33.5 to 51.9)
At least 1 solicited systemic AE (D0-D6)	46.6 (37.2 to 56)	29.5 (21.6 to 38.4)	29.6 (21.4 to 38.8)	26.7 (19 to 35.5)
At least 1 RotaTeq-related solicited systemic AE	44 (34.8 to 53.5)	0 (0 to 0)	27 (19.1 to 36)	0 (0 to 0)
At least 1 MCC-related solicited systemic AE	28.4 (20.5 to 37.6)	23.8 (16.5 to 32.3)	22.6 (15.3 to 31.3)	24.2 (16.8 to 32.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Unsolicited injection-site reactions (ISRs) for MCC vaccine from D0 to D6 following visit 2 and visit 4

End point title	Unsolicited injection-site reactions (ISRs) for MCC vaccine from D0 to D6 following visit 2 and visit 4

End point description:

Unsolicited MCC injection-site adverse reactions (ISRs) were recorded from D0 to D6 following visit 2 (concomitant administration: RotaTeq + MCC vaccine doses 1 / sequential administration: MCC vaccine dose 1 alone) & visit 4 (concomitant administration: RotaTeq + MCC vaccine doses 2 / sequential administration: MCC vaccine dose 2 alone).
AEs at injection sites were always considered as related to MCC vaccine (ISRs).
Analysis was done on the Safety Set at visit 2 (N=238) & Safety Set at visit 4 (N=235), i.e. all subjects who received at least 1 dose of the study vaccines and who had safety follow-up data at visits 2 or 4.

End point type	Secondary

End point timeframe:

Visit 2: from D0 to D6 following visit 2 (concomitant: RotaTeq + MCC vaccine doses 1 / sequential: MCC vaccine dose 1 alone).
Visit 4: from D0 to D6 following visit 4 (concomitant: RotaTeq + MCC vaccine doses 2 / sequential: MCC vaccine dose 2 alone).

End point values	Concomitant administration - visit 2	Sequential administration - visit 2	Concomitant administration - visit 4	Sequential administration - visit 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	116	122	115	120
Units: Percentage of subjects				
number (not applicable)				
Injection-site bruising	0	0.8	0.9	0
Injection-site eczema	0	0	0	0.8
Injection-site erythema	6	4.1	19.1	15.8
Injection-site haematoma	0.9	0	0	0
Injection-site haemorrhage	0	0.8	0	0.8
Injection-site induration	1.7	0.8	2.6	5.8
Injection-site nodule	0	0.8	0	0
Injection-site pain	5.2	2.5	4.3	2.5
Injection-site swelling	1.7	3.3	4.3	5.8

Statistical analyses

No statistical analyses for this end point

Secondary: Solicited systemic AEs from D0 to D6 following visit 2 and visit 4

End point title	Solicited systemic AEs from D0 to D6 following visit 2 and visit 4

End point description:

Solicited systemic AEs (diarrhoea, vomiting & pyrexia: rectal temperature ≥38.1°C or fever without temperature measurement) were recorded daily from D0 to D6 following visit 2 (concomitant administration: RotaTeq + MCC vaccine doses 1 / sequential administration: MCC vaccine dose 1 alone) & visit 4 (concomitant administration: RotaTeq + MCC vaccine doses 2 / sequential administration: MCC vaccine dose 2 alone).
The investigator had to assess whether systemic AEs were vaccine-related systemic AEs or not. All (related and unrelated) are displayed here.
Analysis was done on the Safety Set at visit 2 (N=238) & Safety Set at visit 4 (N=235), i.e. all subjects who received at least 1 dose of the study vaccines and who had safety follow-up data at visits 2 or 4.

End point type	Secondary

End point timeframe:

Visit 2: from D0 to D6 following visit 2 (concomitant: RotaTeq + MCC vaccine doses 1 / sequential: MCC vaccine dose 1 alone).
Visit 4: from D0 to D6 following visit 4 (concomitant: RotaTeq + MCC vaccine doses 2 / sequential: MCC vaccine dose 2 alone).

End point values	Concomitant administration - visit 2	Sequential administration - visit 2	Concomitant administration - visit 4	Sequential administration - visit 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	116	122	115	120
Units: Percentage of subjects				
number (confidence interval 95%)				
Diarrhoea	23.3 (15.9 to 32)	14.8 (9 to 22.3)	13 (7.5 to 20.6)	12.5 (7.2 to 19.8)
Vomiting	19.8 (13 to 28.3)	9.8 (5.2 to 16.6)	10.4 (5.5 to 17.5)	10 (5.3 to 16.8)
Pyrexia	8.6 (4.2 to 15.3)	7.4 (3.4 to 13.5)	18.3 (11.7 to 26.5)	10 (5.3 to 16.8)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited non-serious adverse events (AEs) and all serious AEs were collected from D0 to D13 following each vaccination.
Deaths and vaccine- or procedure-related serious AEs were collected throughout the study.

Adverse event reporting additional description:

Analysis of AEs was performed on the Safety Sets, i.e. all subjects who received at least 1 of the study vaccines and who had safety follow-up data at each visit.
Unsolicited non-serious systemic AEs (vaccine-related or not) with incidence ≥1% in at least 1 reporting group are presented hereafter.
None of the serious AEs were vaccine-related.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Sequential administration - visit 1

Reporting group description:

Subjects who received RotaTeq dose 1 at 6-7 weeks of age (visit 1) and who had safety follow-up data at visit 1.
Respectively, 65 (53.3%) subjects reported at least 1 non-serious unsolicited systemic AE, and 56 (45.9%) subjects reported at least 1 RotaTeq-related non-serious unsolicited systemic AE within 13 days after RotaTeq dose 1.

Reporting group title	Concomitant administration - visit 2

Reporting group description:

Subjects who concomitantly received RotaTeq + MCC vaccine doses 1 at 10-11 weeks of age (visit 2) and who had safety follow-up data at visit 2.
Respectively, 72 (62.1%) subjects reported at least 1 non-serious unsolicited systemic AE, 53 (45.7%) subjects reported at least 1 RotaTeq-related non-serious unsolicited systemic AE, and 57 (49.1%) subjects reported at least 1 MCC vaccine-related non-serious unsolicited systemic AE within 13 days after RotaTeq + MCC vaccine doses 1.

Reporting group title	Sequential administration - visit 2

Reporting group description:

Subjects who received MCC vaccine dose 1 at 10-11 weeks of age (visit 2) and who had safety follow-up data at visit 2.
Respectively, 61 (50.0%) subjects reported at least 1 non-serious unsolicited systemic AE, and 46 (37.7%) subjects reported at least 1 MCC vaccine-related non-serious unsolicited systemic AE within 13 days after MCC vaccine dose 1.

Reporting group title	Sequential administration - visit 3

Reporting group description:

Subjects who received RotaTeq dose 2 at 15-16 weeks of age (visit 3) and who had safety follow-up data at visit 3.
Respectively, 46 (38.3%) subjects reported at least 1 non-serious unsolicited systemic AE, and 27 (22.5%) subjects reported at least 1 RotaTeq-related non-serious unsolicited systemic AE within 13 days after RotaTeq dose 2.

Reporting group title	Concomitant administration - visit 4

Reporting group description:

Subjects who concomitantly received RotaTeq + MCC vaccine doses 2 at 20-21 weeks of age (visit 4) and who had safety follow-up data at visit 4.
Respectively, 47 (40.9%) subjects reported at least 1 non-serious unsolicited systemic AE, 28 (24.3%) subjects reported at least 1 RotaTeq-related non-serious unsolicited systemic AE, and 29 (25.2%) subjects reported at least 1 MCC vaccine-related non-serious unsolicited systemic AE within 13 days after RotaTeq + MCC vaccine doses 2.

Reporting group title	Sequential administration - visit 4

Reporting group description:

Subjects who received MCC vaccine dose 2 at 20-21 weeks of age (visit 4) and who had safety follow-

up data at visit 4.
Respectively, 45 (37.5%) subjects reported at least 1 non-serious unsolicited systemic AE, and 37 (30.8%) subjects reported at least 1 MCC vaccine-related non-serious unsolicited systemic AE within 13 days after MCC vaccine dose 2.

Reporting group title	Concomitant administration - visit 5

Reporting group description:

Subjects who received RotaTeq dose 3 at 24-25 weeks of age (visit 5) and who had safety follow-up data at visit 5.
Note: these subjects previously received RotaTeq and MCC vaccine doses 1 & 2 concomitantly.
Respectively, 25 (22.9%) subjects reported at least 1 non-serious unsolicited systemic AE, and 13 (11.9%) subjects reported at least 1 RotaTeq-related non-serious unsolicited systemic AE within 13 days after RotaTeq dose 3.

Reporting group title	Sequential administration - visit 5

Reporting group description:

Subjects who received RotaTeq dose 3 at 24-25 weeks of age (visit 5) and who had safety follow-up data at visit 5.
Note: these subjects previously received RotaTeq and MCC vaccine doses 1 & 2 sequentially.
Respectively, 26 (22.0%) subjects reported at least 1 non-serious unsolicited systemic AE, and 15 (12.7%) subjects reported at least 1 RotaTeq-related non-serious unsolicited systemic AE within 13 days after RotaTeq dose 3.

Serious adverse events	Sequential administration - visit 1	Concomitant administration - visit 2	Sequential administration - visit 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 122 (0.00%)	0 / 116 (0.00%)	0 / 122 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 122 (0.00%)	0 / 116 (0.00%)	0 / 122 (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			
Viral infection			
subjects affected / exposed	0 / 122 (0.00%)	0 / 116 (0.00%)	0 / 122 (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	Sequential administration - visit 3	Concomitant administration - visit 4	Sequential administration - visit 4
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 120 (0.00%)	1 / 115 (0.87%)	0 / 120 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 120 (0.00%)	1 / 115 (0.87%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 120 (0.00%)	0 / 115 (0.00%)	0 / 120 (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	Concomitant administration - visit 5	Sequential administration - visit 5	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 109 (0.00%)	1 / 118 (0.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 109 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 109 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Sequential administration - visit 1	Concomitant administration - visit 2	Sequential administration - visit 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 122 (53.28%)	72 / 116 (62.07%)	61 / 122 (50.00%)
Nervous system disorders			
Somnolence			

subjects affected / exposed	4 / 122 (3.28%)	8 / 116 (6.90%)	4 / 122 (3.28%)
occurrences (all)	4	8	4
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	13 / 122 (10.66%)	45 / 116 (38.79%)	30 / 122 (24.59%)
occurrences (all)	13	48	32
Pyrexia			
subjects affected / exposed	2 / 122 (1.64%)	2 / 116 (1.72%)	2 / 122 (1.64%)
occurrences (all)	2	2	2
Fatigue			
subjects affected / exposed	1 / 122 (0.82%)	4 / 116 (3.45%)	0 / 122 (0.00%)
occurrences (all)	1	4	0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 122 (0.82%)	1 / 116 (0.86%)	2 / 122 (1.64%)
occurrences (all)	1	1	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	10 / 122 (8.20%)	2 / 116 (1.72%)	5 / 122 (4.10%)
occurrences (all)	10	3	5
Constipation			
subjects affected / exposed	4 / 122 (3.28%)	1 / 116 (0.86%)	2 / 122 (1.64%)
occurrences (all)	4	1	2
Diarrhoea			
subjects affected / exposed	16 / 122 (13.11%)	0 / 116 (0.00%)	2 / 122 (1.64%)
occurrences (all)	19	0	2
Faeces discoloured			
subjects affected / exposed	2 / 122 (1.64%)	2 / 116 (1.72%)	0 / 122 (0.00%)
occurrences (all)	2	2	0
Flatulence			
subjects affected / exposed	16 / 122 (13.11%)	6 / 116 (5.17%)	1 / 122 (0.82%)
occurrences (all)	16	7	1
Regurgitation of food			
subjects affected / exposed	9 / 122 (7.38%)	5 / 116 (4.31%)	1 / 122 (0.82%)
occurrences (all)	9	5	1
Vomiting			

subjects affected / exposed	7 / 122 (5.74%)	0 / 116 (0.00%)	0 / 122 (0.00%)
occurrences (all)	8	0	0
Teething			
subjects affected / exposed	0 / 122 (0.00%)	0 / 116 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	2 / 122 (1.64%)	1 / 116 (0.86%)	1 / 122 (0.82%)
occurrences (all)	2	1	1
Cough			
subjects affected / exposed	0 / 122 (0.00%)	6 / 116 (5.17%)	2 / 122 (1.64%)
occurrences (all)	0	6	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 122 (1.64%)	2 / 116 (1.72%)	1 / 122 (0.82%)
occurrences (all)	2	2	1
Erythema			
subjects affected / exposed	0 / 122 (0.00%)	0 / 116 (0.00%)	2 / 122 (1.64%)
occurrences (all)	0	0	2
Eczema			
subjects affected / exposed	1 / 122 (0.82%)	1 / 116 (0.86%)	1 / 122 (0.82%)
occurrences (all)	1	1	1
Psychiatric disorders			
Crying			
subjects affected / exposed	6 / 122 (4.92%)	6 / 116 (5.17%)	11 / 122 (9.02%)
occurrences (all)	6	7	12
Restlessness			
subjects affected / exposed	0 / 122 (0.00%)	1 / 116 (0.86%)	2 / 122 (1.64%)
occurrences (all)	0	1	2
Infections and infestations			
Rhinitis			
subjects affected / exposed	8 / 122 (6.56%)	5 / 116 (4.31%)	7 / 122 (5.74%)
occurrences (all)	8	6	7
Respiratory tract infection			
subjects affected / exposed	0 / 122 (0.00%)	2 / 116 (1.72%)	0 / 122 (0.00%)
occurrences (all)	0	2	0

Upper respiratory tract infection			
subjects affected / exposed	1 / 122 (0.82%)	3 / 116 (2.59%)	4 / 122 (3.28%)
occurrences (all)	1	3	4
Varicella			
subjects affected / exposed	0 / 122 (0.00%)	0 / 116 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 122 (0.00%)	1 / 116 (0.86%)	0 / 122 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 122 (0.82%)	3 / 116 (2.59%)	0 / 122 (0.00%)
occurrences (all)	1	4	0

Non-serious adverse events	Sequential administration - visit 3	Concomitant administration - visit 4	Sequential administration - visit 4
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 120 (38.33%)	47 / 115 (40.87%)	45 / 120 (37.50%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 120 (0.00%)	2 / 115 (1.74%)	2 / 120 (1.67%)
occurrences (all)	0	2	2
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	9 / 120 (7.50%)	21 / 115 (18.26%)	18 / 120 (15.00%)
occurrences (all)	10	22	21
Pyrexia			
subjects affected / exposed	6 / 120 (5.00%)	1 / 115 (0.87%)	0 / 120 (0.00%)
occurrences (all)	6	1	0
Fatigue			
subjects affected / exposed	0 / 120 (0.00%)	1 / 115 (0.87%)	0 / 120 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctivitis			
subjects affected / exposed	2 / 120 (1.67%)	1 / 115 (0.87%)	2 / 120 (1.67%)
occurrences (all)	2	1	2
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	3 / 120 (2.50%)	2 / 115 (1.74%)	2 / 120 (1.67%)
occurrences (all)	3	2	3
Constipation			
subjects affected / exposed	0 / 120 (0.00%)	0 / 115 (0.00%)	1 / 120 (0.83%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	10 / 120 (8.33%)	0 / 115 (0.00%)	0 / 120 (0.00%)
occurrences (all)	11	0	0
Faeces discoloured			
subjects affected / exposed	1 / 120 (0.83%)	0 / 115 (0.00%)	0 / 120 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	5 / 120 (4.17%)	4 / 115 (3.48%)	1 / 120 (0.83%)
occurrences (all)	5	4	1
Regurgitation of food			
subjects affected / exposed	3 / 120 (2.50%)	0 / 115 (0.00%)	0 / 120 (0.00%)
occurrences (all)	3	0	0
Vomiting			
subjects affected / exposed	4 / 120 (3.33%)	0 / 115 (0.00%)	0 / 120 (0.00%)
occurrences (all)	5	0	0
Teething			
subjects affected / exposed	0 / 120 (0.00%)	6 / 115 (5.22%)	0 / 120 (0.00%)
occurrences (all)	0	6	0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	1 / 120 (0.83%)	0 / 115 (0.00%)	0 / 120 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 120 (0.83%)	0 / 115 (0.00%)	1 / 120 (0.83%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 120 (1.67%)	3 / 115 (2.61%)	5 / 120 (4.17%)
occurrences (all)	2	3	5
Erythema			

subjects affected / exposed	0 / 120 (0.00%)	0 / 115 (0.00%)	1 / 120 (0.83%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	2 / 120 (1.67%)	1 / 115 (0.87%)	0 / 120 (0.00%)
occurrences (all)	2	1	0
Psychiatric disorders			
Crying			
subjects affected / exposed	2 / 120 (1.67%)	6 / 115 (5.22%)	11 / 120 (9.17%)
occurrences (all)	2	6	11
Restlessness			
subjects affected / exposed	0 / 120 (0.00%)	0 / 115 (0.00%)	2 / 120 (1.67%)
occurrences (all)	0	0	2
Infections and infestations			
Rhinitis			
subjects affected / exposed	6 / 120 (5.00%)	3 / 115 (2.61%)	2 / 120 (1.67%)
occurrences (all)	6	3	2
Respiratory tract infection			
subjects affected / exposed	1 / 120 (0.83%)	0 / 115 (0.00%)	0 / 120 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	5 / 120 (4.17%)	1 / 115 (0.87%)	2 / 120 (1.67%)
occurrences (all)	5	1	2
Varicella			
subjects affected / exposed	2 / 120 (1.67%)	0 / 115 (0.00%)	0 / 120 (0.00%)
occurrences (all)	2	0	0
Otitis media			
subjects affected / exposed	0 / 120 (0.00%)	3 / 115 (2.61%)	0 / 120 (0.00%)
occurrences (all)	0	3	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 120 (0.00%)	2 / 115 (1.74%)	2 / 120 (1.67%)
occurrences (all)	0	2	2

Non-serious adverse events	Concomitant administration - visit 5	Sequential administration - visit 5	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 109 (22.94%)	26 / 118 (22.03%)	

Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 109 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	5 / 109 (4.59%)	4 / 118 (3.39%)	
occurrences (all)	5	4	
Pyrexia			
subjects affected / exposed	2 / 109 (1.83%)	5 / 118 (4.24%)	
occurrences (all)	2	5	
Fatigue			
subjects affected / exposed	0 / 109 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	2 / 109 (1.83%)	0 / 118 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 109 (1.83%)	0 / 118 (0.00%)	
occurrences (all)	2	0	
Constipation			
subjects affected / exposed	2 / 109 (1.83%)	0 / 118 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	7 / 109 (6.42%)	7 / 118 (5.93%)	
occurrences (all)	7	7	
Faeces discoloured			
subjects affected / exposed	0 / 109 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	0 / 109 (0.00%)	3 / 118 (2.54%)	
occurrences (all)	0	3	
Regurgitation of food			

subjects affected / exposed	2 / 109 (1.83%)	2 / 118 (1.69%)	
occurrences (all)	2	2	
Vomiting			
subjects affected / exposed	1 / 109 (0.92%)	2 / 118 (1.69%)	
occurrences (all)	1	2	
Teething			
subjects affected / exposed	2 / 109 (1.83%)	3 / 118 (2.54%)	
occurrences (all)	2	3	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 109 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	0 / 109 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	4	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 109 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 109 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	0 / 109 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Crying			
subjects affected / exposed	2 / 109 (1.83%)	0 / 118 (0.00%)	
occurrences (all)	3	0	
Restlessness			
subjects affected / exposed	0 / 109 (0.00%)	2 / 118 (1.69%)	
occurrences (all)	0	2	
Infections and infestations			
Rhinitis			
subjects affected / exposed	5 / 109 (4.59%)	3 / 118 (2.54%)	
occurrences (all)	5	3	

Respiratory tract infection subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1	1 / 118 (0.85%) 1	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 109 (0.92%) 1	0 / 118 (0.00%) 0	
Varicella subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0	0 / 118 (0.00%) 0	
Otitis media subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0	2 / 118 (1.69%) 2	
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all)	0 / 109 (0.00%) 0	1 / 118 (0.85%) 1	

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