Clinical trial results:
A phase III open-label randomised study, to evaluate the immunogenicity and safety of the concomitant administration of V419 (PR5I) given at 2, 3 and 4 months of age with two types of meningococcal serogroup C conjugate (MCC) vaccines given at 3 and 4 months of age, and followed by the administration at 12 months of age of a combined Haemophilus influenzae type b-MCC vaccine.

Summary

EudraCT number	2011-002413-11
Trial protocol	GB
Global end of trial date	27 September 2013

Results information

Result version number	v1
This version publication date	27 April 2016
First version publication date	02 August 2015

Trial information

Trial identification

Sponsor protocol code	PRI01C

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01553279
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	27 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 September 2013
Global end of trial reached?	Yes
Global end of trial date	27 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the concomitant administration of PR5I with 2 types of MCC vaccines (MCC-TT and MCC-CRM) to healthy infants at 3 and 4 months of age in terms of antibody seroprotection rate (SPR) to MCC.

Protection of trial subjects:

Healthy subjects with known or suspected hypersensitivity to any of the study vaccines' component or history of a life-threatening reaction to a vaccine containing the same substances as the study vaccines were excluded.
Vaccines were administered by qualified study personnel.
After each vaccination, subjects were kept under observation for at least 30 minutes to ensure their safety. Adequate treatment provisions, including epinephrine, were to be available for immediate use if an anaphylactic or anaphylactoid reaction occurred.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 March 2012
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	United Kingdom: 284
Worldwide total number of subjects	284
EEA total number of subjects	284

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)	284
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 in 11 active centres in the United Kingdom (UK).

Pre-assignment

Screening details:

292 subjects were screened.
284 subjects were randomised.
282 subjects received all 3 doses of PR5I vaccine and all 2 doses of MCC vaccines (period 1).
281 subjects completed period 1 of the study.
5 subjects discontinued between periods 1 & 2.
276 subjects entered period 2 and received Hib-MCC vaccine.
266 subjects completed the study.

Period 1

Period 1 title	Infant doses
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.
Serology tests were performed by laboratory staffs that were blinded for the group to which each subject was randomised.

Arms

Are arms mutually exclusive?	Yes
Arm title	MCC-TT (period 1)

Arm description:

Subjects received:
3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by intramuscular (IM) route: dose 1 at 2 months of age (Visit 1, V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3).
2 doses of MCC-TT vaccine (NeisVac-C® = Meningococcal group C polysaccharide Conjugate vaccine to tetanus toxoid) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).
As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).
Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-TT vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-TT vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).

Arm type	Experimental
Investigational medicinal product name	PR5I vaccine
Investigational medicinal product code	DTaP-HB-IPV-Hib
Other name	V419
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (left thigh), 3 doses: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2), and dose 3 at 4 months of age (V3).

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

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from PCV-13 vaccine injection-site), 2 doses: dose 1 at 3 months of age (V2), and dose 2 at 4 months of age (V3).

Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	PCV-13 vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from MCC-TT vaccine injection-site), 2 doses: dose 1 at 2 months of age (V1), and dose 2 at 4 months of age (V3).

Arm title	MCC-CRM (period 1)

Arm description:

Subjects received:
3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by IM route: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3).
2 doses of MCC-CRM vaccine (Menjugate® = Meningococcal group C Conjugate vaccine to CRM-197) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).
As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).
Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-CRM vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-CRM vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).

Arm type	Experimental
Investigational medicinal product name	PR5I vaccine
Investigational medicinal product code	DTaP-HB-IPV-Hib
Other name	V419
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (left thigh), 3 doses: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2), and dose 3 at 4 months of age (V3).

Investigational medicinal product name	Menjugate®
Investigational medicinal product code	MCC-CRM vaccine
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from PCV-13 vaccine injection-site), 2 doses: dose 1 at 3 months of age (V2), and dose 2 at 4 months of age (V3).

Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	PCV-13 vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from MCC-CRM vaccine injection-site), 2 doses: dose 1 at 2 months of age (V1), and dose 2 at 4 months of age (V3).

Number of subjects in period 1	MCC-TT (period 1)	MCC-CRM (period 1)
Started	142	142
Completed	140	141
Not completed	2	1
Consent withdrawn by subject	1	1
Lost to follow-up	1	-

Period 2

Period 2 title	Toddler dose
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable as this study was open-label.
Serology tests were performed by laboratory staffs that were blinded for the group to which each subject was randomised.

Arms

Are arms mutually exclusive?	Yes
Arm title	MCC-TT (period 2)

Arm description:

Subjects of the "MCC-TT (period 1)" group received 1 toddler dose of Hib-MCC vaccine (Menitorix® = Haemophilus influenzae type b and Meningococcal group C conjugate vaccine) by IM route at 12 months of age (V5).
As routine vaccination, subjects also received 1 dose of PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) + 1 dose of MMR vaccine (M-M-RvaxPRO® = Measles, Mumps, and Rubella vaccine) by IM route at 12 months of age (V5).
Subjects were blood sampled (i) before toddler dose of Hib-MCC vaccine = Pre Hib-MCC dose (V5), and (ii) 1 month (28-44 days) after toddler dose of Hib-MCC vaccine = Post Hib-MCC dose (V6).

Arm type	Experimental
Investigational medicinal product name	Menitorix®
Investigational medicinal product code	Hib-MCC vaccine
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (left thigh), 1 dose at 12 months of age (V5).

Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	PCV-13 vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from MMR vaccine injection-site), 1 dose at 12 months of age (V5).

Investigational medicinal product name	M-M-RvaxPRO®
Investigational medicinal product code	MMR vaccine
Other name	

Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from PCV-13 vaccine injection-site), 1 dose at 12 months of age (V5).

Arm title	MCC-CRM (period 2)

Arm description:

Subjects of the "MCC-CRM (period 1)" group received 1 toddler dose of Hib-MCC vaccine (Menitorix® = Haemophilus influenzae type b and Meningococcal group C conjugate vaccine) by IM route at 12 months of age (V5).
As routine vaccination, subjects also received 1 dose of PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) + 1 dose of MMR vaccine (M-M-RvaxPRO® = Measles, Mumps, and Rubella vaccine) by IM route at 12 months of age (V5).
Subjects were blood sampled (i) before toddler dose of Hib-MCC vaccine = Pre Hib-MCC dose (V5), and (ii) 1 month (28-44 days) after toddler dose of Hib-MCC vaccine = Post Hib-MCC dose (V6).

Arm type	Experimental
Investigational medicinal product name	Menitorix®
Investigational medicinal product code	Hib-MCC vaccine
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (left thigh), 1 dose at 12 months of age (V5).

Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	PCV-13 vaccine
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from MMR vaccine injection-site), 1 dose at 12 months of age (V5).

Investigational medicinal product name	M-M-RvaxPRO®
Investigational medicinal product code	MMR vaccine
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, IM route (right thigh, separated by at least 5 centimetres from PCV-13 vaccine injection-site), 1 dose at 12 months of age (V5).

Number of subjects in period 2[1]	MCC-TT (period 2)	MCC-CRM (period 2)
Started	137	139
Completed	134	132
Not completed	3	7
Consent withdrawn by subject	-	5
Lost to follow-up	3	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: # In the MCC-TT arm, 3 subjects discontinued the study between the Infant doses and the Toddler dose: 1 "lost of follow-up" and 2 "consent withdrawn by subject".
In the MCC-CRM arm, 2 subjects discontinued the study between the Infant doses and the Toddler dose: 2 "consent withdrawn by subject".

Baseline characteristics

Reporting groups	
Reporting group title	MCC-TT (period 1)
Reporting group description:	
Subjects received: # 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by intramuscular (IM) route: dose 1 at 2 months of age (Visit 1, V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3). # 2 doses of MCC-TT vaccine (NeisVac-C® = Meningococcal group C polysaccharide Conjugate vaccine to tetanus toxoid) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3). # As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3). Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-TT vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-TT vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).	
Reporting group title	MCC-CRM (period 1)
Reporting group description:	
Subjects received: # 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by IM route: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3). # 2 doses of MCC-CRM vaccine (Menjugate® = Meningococcal group C Conjugate vaccine to CRM-197) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3). # As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3). Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-CRM vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-CRM vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).	

Reporting group values	MCC-TT (period 1)	MCC-CRM (period 1)	Total
Number of subjects	142	142	284
Age categorical			
Age at Visit 1.			
Units: Subjects			
Infants and toddlers (mini: 47 days-maxi: 76 days)	142	142	284
Age continuous			
Age in days calculated as (date of vaccination dose 1-date of birth)+1.			
Units: days			
arithmetic mean	62.6	61.6	
standard deviation	± 6.7	± 7.2	-
Gender categorical			
Units: Subjects			
Female	62	67	129
Male	80	75	155

End points

End points reporting groups

Reporting group title	MCC-TT (period 1)

Reporting group description:

Subjects received:
3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by intramuscular (IM) route: dose 1 at 2 months of age (Visit 1, V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3).
2 doses of MCC-TT vaccine (NeisVac-C® = Meningococcal group C polysaccharide Conjugate vaccine to tetanus toxoid) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).
As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).
Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-TT vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-TT vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).

Reporting group title	MCC-CRM (period 1)

Reporting group description:

Subjects received:
3 doses of PR5I vaccine (DTaP-HB-IPV-Hib = Diphtheria, Tetanus, Pertussis (acellular, component), Hepatitis B (rDNA), Poliomyelitis (inactivated) & Haemophilus influenzae type b conjugate vaccine (adsorbed)) by IM route: dose 1 at 2 months of age (V1), dose 2 at 3 months of age (V2) & dose 3 at 4 months of age (V3).
2 doses of MCC-CRM vaccine (Menjugate® = Meningococcal group C Conjugate vaccine to CRM-197) by IM route: dose 1 at 3 months of age (V2) & dose 2 at 4 months of age (V3).
As routine vaccination, subjects also received PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) by IM route: dose 1 at 2 months of age (V1) & dose 2 at 4 months of age (V3).
Subjects were blood sampled (i) before vaccination (V1), (ii) 1 month (28-44 days) Post-Dose 1 of MCC-CRM vaccine (V3) & (iii) 1 month Post-Dose 2 of MCC-CRM vaccine = 1 month Post-Dose 3 of PR5I vaccine (V4).

Reporting group title	MCC-TT (period 2)

Reporting group description:

Subjects of the "MCC-TT (period 1)" group received 1 toddler dose of Hib-MCC vaccine (Menitorix® = Haemophilus influenzae type b and Meningococcal group C conjugate vaccine) by IM route at 12 months of age (V5).
As routine vaccination, subjects also received 1 dose of PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) + 1 dose of MMR vaccine (M-M-RvaxPRO® = Measles, Mumps, and Rubella vaccine) by IM route at 12 months of age (V5).
Subjects were blood sampled (i) before toddler dose of Hib-MCC vaccine = Pre Hib-MCC dose (V5), and (ii) 1 month (28-44 days) after toddler dose of Hib-MCC vaccine = Post Hib-MCC dose (V6).

Reporting group title	MCC-CRM (period 2)

Reporting group description:

Subjects of the "MCC-CRM (period 1)" group received 1 toddler dose of Hib-MCC vaccine (Menitorix® = Haemophilus influenzae type b and Meningococcal group C conjugate vaccine) by IM route at 12 months of age (V5).
As routine vaccination, subjects also received 1 dose of PCV-13 vaccine (Prevenar 13® = Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) + 1 dose of MMR vaccine (M-M-RvaxPRO® = Measles, Mumps, and Rubella vaccine) by IM route at 12 months of age (V5).
Subjects were blood sampled (i) before toddler dose of Hib-MCC vaccine = Pre Hib-MCC dose (V5), and (ii) 1 month (28-44 days) after toddler dose of Hib-MCC vaccine = Post Hib-MCC dose (V6).

Subject analysis set title	Combined vaccine groups
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Combined vaccine groups = MCC-TT period 1 and MCC-CRM period 1 combined groups, i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.

Primary: Acceptability of the seroprotection rate (SPR) to MCC 1 month Post-Dose 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V4)

End point title	Acceptability of the seroprotection rate (SPR) to MCC 1 month Post-Dose 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V4)[1]

End point description:

The SPR to MCC (proportion of subjects with anti-MCC antibody (Ab) titre ≥8 (1/dil)) was determined 1 month Post-Dose 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V4).
Anti-MCC Ab titres were measured by serum bactericidal antibody with rabbit complement (rSBA).
Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.
Note: (N=***, ***) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

End point type	Primary

End point timeframe:

1 month Post-Dose 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V4).

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: There was no comparison between groups in this end point.
The SPR to MCC was considered as acceptable if the lower bounds of the 2-sided 95% CI for the response rates were greater than 90% (i.e., the prespecified acceptability threshold).
Analysis was based on the 2-sided 95% CI with adjustment for multiplicity for single group proportion, calculated using the exact binomial method for binary variables as defined by D. Collet.
Acceptability criteria were met for MCC in both groups.

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	109		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-MCC ≥8 (1/dil) (N=121, 109)	100 (97 to 100)	99.1 (95 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of the SPR to Hib (PRP) 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4)

End point title	Acceptability of the SPR to Hib (PRP) 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4)

End point description:

The SPR to Hib (proportion of subjects with anti-polyribosylribitol phosphate (PRP) Ab titre ≥0.15 µg/mL) was determined 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).
Anti-PRP Ab titres were measured by radioimmunoassay (RIA).
Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.
Acceptability of the SPR to Hib (based on anti-PRP Ab titre ≥0.15 µg/mL) analysis was based on the 2-sided 95% CI for single group proportion, calculated using the exact binomial method for binary variables as defined by D. Collet. If the lower bound of the 2-sided 95% CI was greater than 80% (i.e., the prespecified acceptability threshold), the SPR to Hib was considered as acceptable for the combined vaccine groups. Acceptability criterion was met.

End point type	Secondary

End point timeframe:

1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).

End point values	Combined vaccine groups			
Subject group type	Subject analysis set			
Number of subjects analysed	175			
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-PRP ≥0.15 µg/mL (N=175)	98.9 (95.9 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with anti-MCC Ab titres ≥8 (1/dil) and ≥128 (1/dil) 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4)

End point title	Proportion of subjects with anti-MCC Ab titres ≥8 (1/dil) and ≥128 (1/dil) 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4)

End point description:

Proportion of subjects with anti-MCC Ab titres ≥8 (1/dil) and ≥128 (1/dil) was determined 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4).
Anti-MCC Ab titres were measured by rSBA.
Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.
Note: (N=***, ***) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

End point type	Secondary

End point timeframe:

1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4).

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	109		
Units: Percentage of subjects				
number (confidence interval 95%)				
Post-dose 1 anti-MCC ≥8 (1/dil) (N=102, 84)	100 (96.4 to 100)	96.4 (89.9 to 99.3)		
Post-dose 1 anti-MCC ≥128 (1/dil) (N=102, 84)	98 (93.1 to 99.8)	84.5 (75 to 91.5)		

Post-dose 2 anti-MCC ≥8 (1/dil) (N=121, 109)	100 (97 to 100)	99.1 (95 to 100)		
Post-dose 2 anti-MCC ≥128 (1/dil) (N=121, 109)	99.2 (95.5 to 100)	99.1 (95 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres (GMTs) for MCC 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4)

End point title	Geometric Mean Titres (GMTs) for MCC 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4)

End point description:

Anti-MCC Ab titres were measured by rSBA 1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4).
Ab titres are expressed in 1/dil.
Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.
Note: (N=***, ***) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

End point type	Secondary

End point timeframe:

1 month Post-Dose 1 and 2 of MCC-TT or MCC-CRM vaccine administered concomitantly with PR5I vaccine (V3 and V4).

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	109		
Units: Titres				
geometric mean (confidence interval 95%)				
Post-Dose 1 anti-MCC GMT (N=102, 84)	1353 (1058.4 to 1729.6)	285 (201.5 to 403.1)		
Post-Dose 2 anti-MCC GMT (N=121, 109)	2024.7 (1689.8 to 2425.9)	1077.4 (847.5 to 1369.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ab response rates for all PR5I antigens 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4)

End point title	Ab response rates for all PR5I antigens 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4)

End point description:

% of subjects with an Ab titre ≥0.15 µg/mL for Hib (PRP), ≥10 mIU/mL for Hepatitis B (HBsAg), ≥0.01 & ≥0.1 IU/mL for Diphtheria & Tetanus, ≥8 (1/dil) for Poliovirus types 1, 2 & 3, and % of pertussis seroresponder subjects (Pertussis toxoid (PT), Filamentous haemagglutinin (FHA), Fimbriae types 2 & 3 (FIM) & Pertactin (PRN)) 1 month Post-Dose 3 of PR5I administered concomitantly with MCC vaccines (V4).
Seroresponse was defined: (1) If pre-vaccination Ab concentration (cc) was <LLOQ (lower limit of quantification), post-vaccination Ab cc was to be ≥LLOQ; (2) If pre-vaccination Ab cc was ≥LLOQ, post-vaccination Ab cc was to be ≥pre-immunisation levels.
Ab titres were measured by RIA for PRP, enhanced Chemiluminescence assay (ECi) for HBsAg, micrometabolic inhibition test (MIT) for Diphtheria & Poliovirus, and Enzyme-Linked Immunosorbent Assay (ELISA) for Tetanus, PT, FHA, FIM & PRN.
Analysis was done on the Period 1 PPS.
Note: (N=***, ***) represents the number of assessed subjects.

End point type	Secondary

End point timeframe:

1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	105		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-PRP ≥0.15 µg/mL (N=93, 82)	97.8 (92.4 to 99.7)	100 (95.6 to 100)		
Anti-HBsAg ≥10 mIU/mL (N=93, 82)	96.8 (90.9 to 99.3)	96.3 (89.7 to 99.2)		
Anti-Diphtheria ≥0.01 IU/mL (N=125, 104)	100 (97.1 to 100)	100 (96.5 to 100)		
Anti-Diphtheria ≥0.1 IU/mL (N=125, 104)	68 (59.1 to 76.1)	74 (64.5 to 82.1)		
Anti-Tetanus ≥0.01 IU/mL (N=122, 105)	100 (97 to 100)	100 (96.5 to 100)		
Anti-Tetanus ≥0.1 IU/mL (N=122, 105)	100 (97 to 100)	100 (96.5 to 100)		
Anti-PT seroresponse (N=100, 75)	99 (94.6 to 100)	100 (95.2 to 100)		
Anti-FHA seroresponse (N=100, 74)	91 (83.6 to 95.8)	90.5 (81.5 to 96.1)		
Anti-PRN seroresponse (N=100, 73)	95 (88.7 to 98.4)	90.4 (81.2 to 96.1)		
Anti-FIM seroresponse (N=100, 75)	96 (90.1 to 98.9)	96 (88.8 to 99.2)		
Anti-Polio 1 ≥8 (1/dil) (N=114, 95)	100 (96.8 to 100)	100 (96.2 to 100)		
Anti-Polio 2 ≥8 (1/dil) (N=106, 89)	100 (96.6 to 100)	100 (95.9 to 100)		
Anti-Polio 3 ≥8 (1/dil) (N=90, 74)	100 (96 to 100)	100 (95.1 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres (GMTs) for all PR5I antigens 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4)

End point title	Geometric Mean Titres (GMTs) for all PR5I antigens 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4)

End point description:

Ab titres were measured by RIA for Hib (PRP), ECi for HBsAg, MIT for Diphtheria & Poliovirus, and ELISA for Tetanus, PT, FHA, FIM & PRN 1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).
Ab titres are expressed in µg/mL for Hib (PRP), mIU/mL for HBsAg, IU/mL for Diphtheria & Tetanus, ELISA units (EU)/mL for Pertussis (PT, FHA, FIM & PRN), and 1/dil for Poliovirus types 1, 2 & 3.
Analysis was done on the Period 1 Per Protocol Set (PPS), i.e., all randomised subjects excluding those with protocol deviation which could interfere with the immunogenicity evaluation.
Note: (N=***, ***) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

End point type	Secondary

End point timeframe:

1 month Post-Dose 3 of PR5I vaccine administered concomitantly with MCC-TT or MCC-CRM vaccine (V4).

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125	105		
Units: Titres				
geometric mean (confidence interval 95%)				
Anti-PRP GMT (N=93, 82)	6.44 (4.7 to 8.83)	8.21 (6.08 to 11.09)		
Anti-HBsAg GMT (N=93, 82)	195.1 (150.7 to 252.7)	247.7 (186.3 to 329.3)		
Anti-Diphtheria GMT (N=125, 104)	0.198 (0.165 to 0.237)	0.22 (0.181 to 0.268)		
Anti-Tetanus GMT (N=122, 105)	1.03 (0.9 to 1.17)	0.95 (0.82 to 1.1)		
Anti-PT GMT (N=112, 89)	131.5 (117.2 to 147.6)	133.3 (118.3 to 150.2)		
Anti-FHA GMT (N=112, 88)	50.4 (44.8 to 56.6)	50.1 (43.7 to 57.4)		
Anti-PRN GMT (N=112, 87)	90.4 (73.2 to 111.7)	106.8 (83.7 to 136.3)		
Anti-FIM GMT (N=112, 89)	401.7 (339.4 to 475.5)	441.7 (363.2 to 537.2)		
Anti-Polio 1 GMT (N=114, 95)	214 (164.9 to 277.7)	257.9 (193.8 to 343.1)		
Anti-Polio 2 GMT (N=106, 89)	385.2 (288.2 to 514.9)	400.6 (290.6 to 552.3)		
Anti-Polio 3 GMT (N=90, 74)	502.2 (370.2 to 681.4)	405.1 (284.9 to 576)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with anti-MCC Ab titres ≥8 (1/dil) and ≥128 (1/dil) before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

End point title	Proportion of subjects with anti-MCC Ab titres ≥8 (1/dil) and ≥128 (1/dil) before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

End point description:

Proportion of subjects with anti-MCC Ab titres ≥8 (1/dil) and ≥128 (1/dil) determined before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).
Anti-MCC Ab titres were measured by rSBA.
Analysis was done on the Period 2 Per Protocol Set (PPS), i.e., all randomised subjects vaccinated in period 2, excluding those with protocol deviation which could interfere with the immunogenicity evaluation.
Note: (N=***, ***) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

End point type	Secondary

End point timeframe:

Before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).

End point values	MCC-TT (period 2)	MCC-CRM (period 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	110		
Units: Percentage of subjects				
number (confidence interval 95%)				
Pre Hib-MCC anti-MCC ≥8 (1/dil) (N=89, 94)	83.1 (73.7 to 90.2)	40.4 (30.4 to 51)		
Pre Hib-MCC anti-MCC ≥128 (1/dil) (N=89, 94)	40.4 (30.2 to 51.4)	16 (9.2 to 25)		
Post Hib-MCC anti-MCC ≥8 (1/dil) (N=109, 110)	100 (96.7 to 100)	97.3 (92.2 to 99.4)		
Post Hib-MCC anti-MCC ≥128 (1/dil) (N=109, 110)	99.1 (95 to 100)	95.5 (89.7 to 98.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres (GMTs) for MCC before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

End point title	Geometric Mean Titres (GMTs) for MCC before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

End point description:

Anti-MCC Ab titres were measured by rSBA before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).
Ab titres are expressed in 1/dil.
Analysis was done on the Period 2 Per Protocol Set (PPS), i.e., all randomised subjects vaccinated in period 2, excluding those with protocol deviation which could interfere with the immunogenicity

evaluation.
Note: (N=***, ***) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

End point type	Secondary

End point timeframe:

Before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).

End point values	MCC-TT (period 2)	MCC-CRM (period 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	110		
Units: Titres				
geometric mean (confidence interval 95%)				
Pre Hib-MCC dose anti-MCC GMT (N=89, 94)	50.3 (34.4 to 73.4)	8.7 (5.9 to 12.9)		
Post Hib-MCC dose anti-MCC GMT (N=109, 110)	3257.9 (2597.4 to 4086.3)	580.8 (432.7 to 779.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects with anti-PRP Ab titres ≥0.15 µg/mL and ≥1.0 µg/mL before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

End point title	Proportion of subjects with anti-PRP Ab titres ≥0.15 µg/mL and ≥1.0 µg/mL before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

End point description:

Proportion of subjects with anti-PRP Ab titres ≥0.15 µg/mL and ≥1.0 µg/mL determined before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).
Anti-PRP Ab titres were measured by radioimmunoassay (RIA).
Analysis was done on the Period 2 Per Protocol Set (PPS), i.e., all randomised subjects vaccinated in period 2, excluding those with protocol deviation which could interfere with the immunogenicity evaluation.
Note: (N=***, ***) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

End point type	Secondary

End point timeframe:

Before (Pre Hib-MCC dose, V5) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose, V6).

End point values	MCC-TT (period 2)	MCC-CRM (period 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	106		
Units: Percentage of subjects				
number (confidence interval 95%)				
Pre Hib-MCC anti-PRP ≥0.15 µg/mL (N=82, 87)	93.9 (86.3 to 98)	95.4 (88.6 to 98.7)		
Pre Hib-MCC anti-PRP ≥1.0 µg/mL (N=82, 87)	54.9 (43.5 to 65.9)	56.3 (45.3 to 66.9)		
Post Hib-MCC anti-PRP ≥0.15 µg/mL (N=110, 106)	100 (96.7 to 100)	100 (96.6 to 100)		
Post Hib-MCC anti-PRP ≥1.0 µg/mL (N=110, 106)	99.1 (95 to 100)	100 (96.6 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres (GMTs) for Hib (PRP) before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

End point title	Geometric Mean Titres (GMTs) for Hib (PRP) before (Pre, V5) and 1 month after (Post, V6) Hib-MCC vaccine dose

End point description:

Anti-PRP Ab titres were measured by RIA before (Pre Hib-MCC dose) and 1 month after Hib-MCC vaccine toddler dose administration (Post Hib-MCC dose).
Ab titres are expressed in µg/mL.
Analysis was done on the Period 2 Per Protocol Set (PPS), i.e., all randomised subjects vaccinated in period 2, excluding those with protocol deviation which could interfere with the immunogenicity evaluation.
Note: (N=***, ***) represents the number of assessed subjects in the "MCC-TT" and "MCC-CRM" groups, respectively.

End point type	Secondary

End point timeframe:

Before (Pre Hib-MCC dose) and 1 month after Hib-MCC toddler dose administration (Post Hib-MCC dose).

End point values	MCC-TT (period 2)	MCC-CRM (period 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	106		
Units: Titres				
geometric mean (confidence interval 95%)				
Pre Hib-MCC dose anti-PRP GMT (N=82, 87)	1.09 (0.81 to 1.45)	1.18 (0.9 to 1.55)		
Post Hib-MCC dose anti-PRP GMT (N=110, 106)	100.19 (81.05 to 123.86)	121 (101.11 to 144.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Global summary of safety from D1 to D15 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine)

End point title	Global summary of safety from D1 to D15 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine)

End point description:

Adverse events (AEs) were recorded as follows:
1/ From D1 to D5 after each vaccination: # temperature (at least 1 ≥38.0°C), # solicited injection-site adverse reactions (ISRs: erythema, pain, and swelling) by injection-site (PR5I or MCC vaccine), and # solicited systemic AEs (crying, decreased appetite, irritability, pyrexia, somnolence, and vomiting).
2/ From D1 to D15 after each vaccination: unsolicited ISRs (including erythema, pain, and swelling from D6 to D15) by injection-site (PR5I or MCC vaccine), and # unsolicited systemic AEs.
AEs at injection sites were always considered as related to vaccine (ISRs). The investigator had to assess whether systemic AEs were vaccine-related systemic AEs or not.
Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.
Percentages of subjects reporting AEs that occurred after any infant dose vaccination are presented herafter.

End point type	Secondary

End point timeframe:

From Day 1 (D1) to D15 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine).

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	142		
Units: Percentage of subjects				
number (confidence interval 95%)				
At least 1 AE (D1-D15)	98.6 (95 to 99.8)	97.2 (92.9 to 99.2)		
At least 1 vaccine-related AE (D1-D15)	98.6 (95 to 99.8)	96.5 (92 to 98.8)		
At least 1 ISR at PR5I site (D1-D15)	88.7 (82.3 to 93.4)	87.3 (80.7 to 92.3)		
At least 1 solicited ISR at PR5I site (D1-D5)	88.7 (82.3 to 93.4)	87.3 (80.7 to 92.3)		
At least 1 unsolicited ISR at PR5I site (D1-D15)	6.3 (2.9 to 11.7)	11.3 (6.6 to 17.7)		
At least 1 ISR at MCC site (D1-D15)	72.5 (64.4 to 79.7)	66.2 (57.8 to 73.9)		
At least 1 solicited ISR at MCC site (D1-D5)	72.5 (64.4 to 79.7)	65.5 (57.1 to 73.3)		
At least 1 unsolicited ISR at MCC site (D1-D15)	2.8 (0.8 to 7.1)	2.8 (0.8 to 7.1)		
At least 1 systemic AE (D1-D15)	98.6 (95 to 99.8)	94.4 (89.2 to 97.5)		
At least 1 vaccine-related systemic AE (D1-D15)	97.9 (94 to 99.6)	93.7 (88.3 to 97.1)		
At least 1 solicited systemic AE (D1-D5)	97.2 (92.9 to 99.2)	93 (87.4 to 99.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects reporting ISRs at PR5I injection-site from D1 to D5 (solicited) or D1 to D15 (unsolicited) after any infant dose vaccination (3 doses of PR5I vaccine)

End point title	Percentage of subjects reporting ISRs at PR5I injection-site from D1 to D5 (solicited) or D1 to D15 (unsolicited) after any infant dose vaccination (3 doses of PR5I vaccine)

End point description:

ISRs occurring after any infant dose of PR5I vaccine (3 doses) were recorded as follows:
From D1 to D5 after each vaccination: solicited ISRs, i.e., erythema, pain, and swelling at PR5I injection-site.
From D1 to D15 after each vaccination: unsolicited ISRs (including erythema, pain, and swelling from D6 to D15) at PR5I injection-site.
AEs at injection-site were always considered as related to vaccine (ISRs).
The percentage of subjects presenting at least once the following ISRs that occurred after any infant dose vaccination is reported hereafter.
Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

End point type	Secondary

End point timeframe:

Solicited ISRs: from Day 1 (D1) to D5 after any infant dose of PR5I vaccine (3 doses).
Unsolicited ISRs: from Day 1 (D1) to D15 after any infant dose of PR5I vaccine (3 doses).

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	142		
Units: Percentage of subjects				
number (not applicable)				
Solicited injection-site erythema (D1-D5)	71.1	64.8		
Solicited injection-site pain (D1-D5)	63.4	66.2		
Solicited injection-site swelling (D1-D5)	51.4	47.2		
Unsolicited injection-site bruising (D1-D15)	1.4	4.2		
Unsolicited injection-site dermatitis (D1-D15)	0	0.7		
Unsolicited injection-site erythema (D6-D15)	0	0.7		
Unsolicited injection-site induration (D1-D15)	1.4	0.7		
Unsolicited injection-site mass (D1-D15)	3.5	2.1		
Unsolicited injection-site pain (D6-D15)	0	0.7		
Unsolicited injection-site rash (D1-D15)	1.4	0.7		

Unsolicited injection-site warmth (D1-D15)	0	2.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects reporting ISRs at MCC-TT or MCC-CRM injection-site from D1 to D5 (solicited) or D1 to D15 (unsolicited) after any infant dose vaccination (2 doses of MCC-TT or MCC-CRM vaccine)

End point title	Percentage of subjects reporting ISRs at MCC-TT or MCC-CRM injection-site from D1 to D5 (solicited) or D1 to D15 (unsolicited) after any infant dose vaccination (2 doses of MCC-TT or MCC-CRM vaccine)

End point description:

ISRs occurring after any infant dose of MCC-TT or MCC-CRM vaccine (2 doses) were recorded as follows:
From D1 to D5: solicited ISRs, i.e., erythema, pain, and swelling at MCC injection-site.
From D1 to D15: unsolicited ISRs (including erythema, pain, and swelling from D6 to D15) at MCC injection-site.
AEs at injection-site were always considered as related to vaccine (ISRs).
The percentage of subjects presenting at least once the following ISRs that occurred after any infant dose vaccination is reported hereafter.
Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

End point type	Secondary

End point timeframe:

Solicited ISRs: from Day 1 (D1) to D5 after any infant dose of MCC-TT or MCC-CRM vaccine (2 doses).
Unsolicited ISRs: from Day 1 (D1) to D15 after any infant dose of MCC-TT or MCC-CRM vaccine (2 doses).

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	142		
Units: Percentage of subjects				
number (not applicable)				
Solicited injection-site erythema (D1-D5)	56.3	45.8		
Solicited injection-site pain (D1-D5)	41.5	45.8		
Solicited injection-site swelling (D1-D5)	35.9	28.2		
Unsolicited injection-site bruising (D1-D15)	1.4	2.1		
Unsolicited injection-site induration (D1-D15)	0.7	0		
Unsolicited injection-site rash (D1-D15)	0.7	0		
Unsolicited injection-site warmth (D1-D15)	0	0.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects reporting solicited systemic adverse events (AEs) from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine)

End point title	Percentage of subjects reporting solicited systemic adverse events (AEs) from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine)

End point description:

Solicited systemic AEs (crying, decreased appetite, irritability, pyrexia, somnolence, and vomiting) were recorded from D1 to D5 after each vaccination.
The investigator had to assess whether systemic AEs were vaccine-related systemic AEs or not.
The percentage of subjects presenting at least once the following solicited systemic AEs (vaccine-related or not) that occurred after any infant dose vaccination is presented herafter.
Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

End point type	Secondary

End point timeframe:

From Day 1 (D1) to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine).

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	142		
Units: Percentage of subjects				
number (not applicable)				
Crying (D1-D5)	85.9	81		
Decreased appetite (D1-D5)	63.4	64.8		
Irritability (D1-D5)	88	81		
Pyrexia (D1-D5)	11.3	10.6		
Somnolence (D1-D5)	81.7	78.9		
Vomiting (D1-D5)	40.1	49.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects reporting temperature ≥38.0°C, >38.5°C & >39.5°C from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine)

End point title	Percentage of subjects reporting temperature ≥38.0°C, >38.5°C & >39.5°C from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine)

End point description:

Maximum temperatures recorded with no adjustments to the measurement route were reported from D1 to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine).

The percentage of subjects presenting at least once temperature ≥38.0°C, >38.5°C, and >39.5°C is presented hereafter.
Analysis was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.

End point type	Secondary

End point timeframe:

From Day 1 (D1) to D5 after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT or MCC-CRM vaccine).

End point values	MCC-TT (period 1)	MCC-CRM (period 1)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	142		
Units: Percentage of subjects				
number (not applicable)				
Temperature ≥38.0°C	11.3	10.6		
Temperature >38.5°C	1.4	2.1		
Temperature >39.5°C	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From D1 to D15 after each vaccination during Period 1: unsolicited non-serious systemic AEs.
From D1 to D15 after each vaccination: serious AEs (SAEs) and deaths, vaccine-related or not.
Throughout the study: deaths and vaccine-related SAEs.

Adverse event reporting additional description:

Analysis of AEs was done on the Period 1 Safety Set, i.e., all subjects who received at least 1 study vaccine during period 1 and who had safety follow-up data in period 1.
Unsolicited non-serious systemic AEs (vaccine-related or not) with incidence ≥2% are presented hereafter.
1 subject from the MCC-CRM group reported 2 vaccine-related SAEs.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	MCC-TT (period 1)

Reporting group description:

Subjects received 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib) by IM route at 2, 3, & 4 months of age + 2 doses of MCC-TT vaccine (NeisVac-C) by IM route at 3 & 4 months of age + routine vaccination, i.e., PCV-13 vaccine (Prevenar 13) by IM route at 2 & 4 months of age.
Respectively, 71 (50.0%) subjects reported at least 1 unsolicited systemic AE, and 38 (26.8%) subjects reported at least 1 vaccine-related unsolicited systemic AE within 15 days after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-TT vaccine).

Reporting group title	MCC-CRM (period 1)

Reporting group description:

Subjects received 3 doses of PR5I vaccine (DTaP-HB-IPV-Hib) by IM route at 2, 3 & 4 months of age + 2 doses of MCC-CRM vaccine (Menjugate) by IM route at 3 & 4 months of age + routine vaccination, i.e., PCV-13 vaccine (Prevenar 13) by IM route at 2 & 4 months of age.
Respectively, 57 (40.1%) subjects reported at least 1 unsolicited systemic AE, and 37 (26.1%) subjects reported at least 1 vaccine-related unsolicited systemic AE within 15 days after any infant dose vaccination (3 doses of PR5I vaccine and 2 doses of MCC-CRM vaccine).

Serious adverse events	MCC-TT (period 1)	MCC-CRM (period 1)	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 142 (4.23%)	4 / 142 (2.82%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Crying	Additional description: Transient (2 days), severe intensity, occurring concomitantly with abdominal pain in 1 subject.		
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothermia			

subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain	Additional description: Transient (2 days), severe intensity, occurring concomitantly with crying in 1 subject.		
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Croup infectious			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	
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	0 / 142 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis neonatal			

subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Weight gain poor			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	MCC-TT (period 1)	MCC-CRM (period 1)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 142 (50.00%)	57 / 142 (40.14%)	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 142 (0.00%)	3 / 142 (2.11%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	4 / 142 (2.82%)	3 / 142 (2.11%)	
occurrences (all)	4	3	
Diarrhoea			
subjects affected / exposed	11 / 142 (7.75%)	8 / 142 (5.63%)	
occurrences (all)	11	8	
Teething			
subjects affected / exposed	7 / 142 (4.93%)	1 / 142 (0.70%)	
occurrences (all)	7	1	
Vomiting			
subjects affected / exposed	3 / 142 (2.11%)	3 / 142 (2.11%)	
occurrences (all)	3	3	

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 142 (8.45%)	6 / 142 (4.23%)	
occurrences (all)	12	6	
Nasal congestion			
subjects affected / exposed	4 / 142 (2.82%)	2 / 142 (1.41%)	
occurrences (all)	4	2	
Rhinorrhoea			
subjects affected / exposed	3 / 142 (2.11%)	4 / 142 (2.82%)	
occurrences (all)	3	4	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	8 / 142 (5.63%)	6 / 142 (4.23%)	
occurrences (all)	8	6	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 142 (2.82%)	1 / 142 (0.70%)	
occurrences (all)	4	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 142 (7.75%)	12 / 142 (8.45%)	
occurrences (all)	11	12	
Rhinitis			
subjects affected / exposed	8 / 142 (5.63%)	6 / 142 (4.23%)	
occurrences (all)	8	6	

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