



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 | v2 (current) |
| This version publication date | 16 November 2019 |
| First version publication date | 02 August 2015 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | V419-011 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01553279 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | PRI01C: Sanofi Protocol Pasteur MSD Protocol Number |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Senior Vice President, Global Clinical Development, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Senior Vice President, Global Clinical Development, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |

Notes:

Paediatric regulatory details

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|--|-----|
| 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:

The primary objectives of this study are to evaluate the immunogenicity and safety of concomitant administration of V419 (PR51) with 2 types of meningococcal serogroup C conjugate (MCC) vaccines to healthy infants at 3 and 4 months of age in terms of antibody seroprotection rate (SPR) to MCC. Participants also received a Haemophilus influenza type B (Hib)-MCC vaccination at 12 months of age. It was hypothesized that the SPR to MCC at 1 month post-dose 2 of either tetanus toxoid conjugated Meningo C (MCC-TT) or CRM197 conjugated Meningo C (MCC-CRM) vaccines would be acceptable when administered concomitantly with V419.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 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: -

Pre-assignment

Screening details:

Infant participants were enrolled at 11 study sites in the United Kingdom.

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Part 1: Infant Vaccinations |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | V419 and MCC-TT |

Arm description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-TT (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 3 doses of Prevnar 13® (at 2, 4, and 12 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | V419 |
| Investigational medicinal product code | |
| Other name | PR51; VAXELIS® |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Diphtheria and Tetanus toxoids and acellular Pertussis adsorbed, inactivated Poliovirus, Haemophilus b conjugate [meningococcal outer membrane protein complex], and Hepatitis B [recombinant] vaccine administered via 0.5 mL intramuscular injection.

| | |
|--|--------------------------|
| Investigational medicinal product name | PREVNAR 13® |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Pneumococcal conjugate vaccine (13-valent, adsorbed) administered via 0.5 mL intramuscular injection (routine vaccination).

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

Dosage and administration details:

Meningococcal Group C polysaccharide conjugate vaccine to tetanus toxoid adsorbed 0.5 mL intramuscular injection at 3 and 4 months of age.

| | |
|--|------------------------|
| Investigational medicinal product name | Hib-MCC |
| Investigational medicinal product code | |
| Other name | MENITORIX® |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Haemophilus type b and meningococcal Group C conjugate vaccine administered via 0.5 mL intramuscular injection.

| | |
|------------------|------------------|
| Arm title | V419 and MCC-CRM |
|------------------|------------------|

Arm description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-CRM (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 3 doses of Prevnar 13® (at 2, 4, and 12 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | V419 |
| Investigational medicinal product code | |
| Other name | PR51; VAXELIS® |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Diphtheria and Tetanus toxoids and acellular Pertussis adsorbed, inactivated Poliovirus, Haemophilus b conjugate [meningococcal outer membrane protein complex], and Hepatitis B [recombinant] vaccine administered via 0.5 mL intramuscular injection.

| | |
|--|--------------------------|
| Investigational medicinal product name | MCC-CRM |
| Investigational medicinal product code | |
| Other name | MENJUGATE® |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Meningococcal Group C conjugate vaccine to CRM-197 adsorbed 0.5 mL intramuscular injection at 3 and 4 months of age.

| | |
|--|------------------------|
| Investigational medicinal product name | Hib-MCC |
| Investigational medicinal product code | |
| Other name | MENITORIX® |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Haemophilus type b and meningococcal Group C conjugate vaccine administered via 0.5 mL intramuscular injection.

| | |
|--|--------------------------|
| Investigational medicinal product name | PREVNAR 13® |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Pneumococcal conjugate vaccine (13-valent, adsorbed) administered via 0.5 mL intramuscular injection (routine vaccination).

| Number of subjects in period 1 | V419 and MCC-TT | V419 and MCC-CRM |
|--------------------------------|-----------------|------------------|
| 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 | Interim Period |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

No study drug was administered during the Interim Period.

Arms

| | |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | V419 and MCC-TT |

Arm description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-TT (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| | |
|----------|-----------------|
| Arm type | No intervention |
|----------|-----------------|

No investigational medicinal product assigned in this arm

| | |
|------------------|------------------|
| Arm title | V419 and MCC-CRM |
|------------------|------------------|

Arm description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-CRM (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| | |
|----------|-----------------|
| Arm type | No intervention |
|----------|-----------------|

No investigational medicinal product assigned in this arm

| Number of subjects in period 2 | V419 and MCC-TT | V419 and MCC-CRM |
|--------------------------------|-----------------|------------------|
| Started | 140 | 141 |
| Completed | 137 | 139 |
| Not completed | 3 | 2 |
| Consent withdrawn by subject | 2 | 2 |
| Lost to follow-up | 1 | - |

Period 3

| | |
|------------------------------|--------------------------------|
| Period 3 title | Period 2: Toddler Vaccinations |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | V419 and MCC-TT |

Arm description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-TT (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Hib-MCC |
| Investigational medicinal product code | |
| Other name | MENITORIX® |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Haemophilus type b and meningococcal Group C conjugate vaccine administered via 0.5 mL intramuscular injection.

| | |
|--|--------------------------|
| Investigational medicinal product name | MMR Vaccine |
| Investigational medicinal product code | |
| Other name | M-M-RVAXPRO® |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Measles, mumps, and rubella vaccine (live) given via 0.5 mL intramuscular injection (routine vaccination).

| | |
|------------------|------------------|
| Arm title | V419 and MCC-CRM |
|------------------|------------------|

Arm description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-CRM (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MMR Vaccine |
| Investigational medicinal product code | |
| Other name | M-M-RVAXPRO® |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Measles, mumps, and rubella vaccine (live) given via 0.5 mL intramuscular injection (routine vaccination).

| | |
|--|------------------------|
| Investigational medicinal product name | Hib-MCC |
| Investigational medicinal product code | |
| Other name | MENITORIX® |
| Pharmaceutical forms | Solution for injection |

| | |
|--------------------------|-------------------|
| Routes of administration | Intramuscular use |
|--------------------------|-------------------|

Dosage and administration details:

Haemophilus type b and meningococcal Group C conjugate vaccine administered via 0.5 mL intramuscular injection.

| Number of subjects in period 3 | V419 and MCC-TT | V419 and MCC-CRM |
|---------------------------------------|-----------------|------------------|
| Started | 137 | 139 |
| Completed | 134 | 132 |
| Not completed | 3 | 7 |
| Consent withdrawn by subject | - | 5 |
| Lost to follow-up | 3 | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | V419 and MCC-TT |
|-----------------------|-----------------|

Reporting group description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-TT (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 3 doses of Prevnar 13® (at 2, 4, and 12 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| | |
|-----------------------|------------------|
| Reporting group title | V419 and MCC-CRM |
|-----------------------|------------------|

Reporting group description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-CRM (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 3 doses of Prevnar 13® (at 2, 4, and 12 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| Reporting group values | V419 and MCC-TT | V419 and MCC-CRM | Total |
|--|-----------------|------------------|-------|
| Number of subjects | 142 | 142 | 284 |
| Age categorical Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 142 | 142 | 284 |
| Age Continuous Units: Days | | | |
| arithmetic mean | 62.6 | 61.6 | |
| standard deviation | ± 6.7 | ± 7.2 | - |
| Sex: Female, Male Units: Subjects | | | |
| Female | 62 | 67 | 129 |
| Male | 80 | 75 | 155 |

End points

End points reporting groups

| | |
|---|-----------------------|
| Reporting group title | V419 and MCC-TT |
| Reporting group description: In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-TT (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 3 doses of Prevnar 13® (at 2, 4, and 12 months of age) and 1 dose of an MMR vaccine (at 12 months of age). | |
| Reporting group title | V419 and MCC-CRM |
| Reporting group description: In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-CRM (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 3 doses of Prevnar 13® (at 2, 4, and 12 months of age) and 1 dose of an MMR vaccine (at 12 months of age). | |
| Reporting group title | V419 and MCC-TT |
| Reporting group description: In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-TT (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age). | |
| Reporting group title | V419 and MCC-CRM |
| Reporting group description: In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-CRM (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age). | |
| Reporting group title | V419 and MCC-TT |
| Reporting group description: In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-TT (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age). | |
| Reporting group title | V419 and MCC-CRM |
| Reporting group description: In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-CRM (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age). | |
| Subject analysis set title | V419 + MCC-TT/MCC-CRM |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Pooled population of participants who received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of either MCC-TT or MCC-CRM (at 3 and 4 months of age) in Part 1. | |

Primary: Percentage of Participants with Anti-Meningococcal Serogroup C (anti-MCC) Antibody (Ab) Titre $\geq 1:8$ dil One Month After MCC-TT or MCC-CRM (Part 1)

| | |
|--|--|
| End point title | Percentage of Participants with Anti-Meningococcal Serogroup C (anti-MCC) Antibody (Ab) Titre $\geq 1:8$ dil One Month After MCC-TT or MCC-CRM (Part 1) ^[1] |
| End point description: The acceptability (i.e., percentage of participants with anti-MCC Ab titre $\geq 1:8$ dil) of the seroprotection rate (SPR) to MCC was determined 1 month after MCC-TT or MCC-CRM Dose 2. The SPR was considered acceptable if the lower bound of the 2-sided 95% CI was $>90\%$. Serum Ab levels were assayed using the Meningo C rabbit complement serum bactericidal Ab (rSBA) assay. All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included. | |
| End point type | Primary |

End point timeframe:

Month 5 (1 month after MCC-TT/MCC-CRM Dose 2)

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: Per protocol, only descriptive statistics are presented.

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|-----------------------------------|-----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 121 | 109 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 100.0 (97.0 to 100.0) | 99.1 (95.0 to 100.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Anti-Polyribosylribitol Phosphate (anti-PRP) Antibody (Ab) Titre ≥ 0.15 $\mu\text{g/mL}$ One Month After V419 Dose 3 (Part 1)

| | |
|-----------------|--|
| End point title | Percentage of Participants with Anti-Polyribosylribitol Phosphate (anti-PRP) Antibody (Ab) Titre ≥ 0.15 $\mu\text{g/mL}$ One Month After V419 Dose 3 (Part 1) |
|-----------------|--|

End point description:

The acceptability (i.e., percentage of participants with anti-PRP Ab titre ≥ 0.15 $\mu\text{g/mL}$) of the seroprotection rate (SPR) to Haemophilus influenza type b (Hib) was determined 1 month after the third dose of V419 in participants also treated with MCC-TT or MCC-CRM. The pooled (i.e., all V419-treated participants) SPR was considered acceptable if the lower bound of the 2-sided 95% CI was $>80\%$. Serum Ab levels were determined with radioimmunoassay (RIA). All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 5 (1 month after V419 Dose 3)

| End point values | V419 + MCC-TT/MCC-CRM | | | |
|-----------------------------------|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 175 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 98.9 (95.9 to 99.9) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Anti-Meningococcal Serogroup C (anti-

MCC) Antibody (Ab) Titre $\geq 1:8$ dil and $\geq 1:128$ dil One Month After MCC-TT or MCC-CRM Doses 1 and 2 (Part 1)

| | |
|-----------------|--|
| End point title | Percentage of Participants with Anti-Meningococcal Serogroup C (anti-MCC) Antibody (Ab) Titre $\geq 1:8$ dil and $\geq 1:128$ dil One Month After MCC-TT or MCC-CRM Doses 1 and 2 (Part 1) |
|-----------------|--|

End point description:

The percentage of participants with anti-MCC Ab titres $\geq 1:8$ dil and $\geq 1:128$ dil 1 month after MCC-TT or MCC-CRM Doses 1 and 2 was determined in participants also treated with V419. Serum Ab levels were assayed using the Meningo C rabbit complement serum bactericidal Ab (rSBA) assay. All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 4 and Month 5 (1 month after MCC-TT/MCC-CRM Doses 1 and 2)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|---|-----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 121 | 109 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Post-MCC Dose 1: % with $\geq 1:8$ dil (n=102, 84) | 100.0 (96.4 to 100.0) | 96.4 (89.9 to 99.3) | | |
| Post-MCC Dose 1: % with $\geq 1:128$ dil (n=102, 84) | 98.0 (93.1 to 99.8) | 84.5 (75.0 to 91.5) | | |
| Post-MCC Dose 2: % with $\geq 1:8$ dil (n=121, 109) | 100.0 (97.0 to 100.0) | 99.1 (95.0 to 100.0) | | |
| Post-MCC Dose 2: % with $\geq 1:128$ dil (n=121, 109) | 99.2 (95.5 to 100.0) | 99.1 (95.0 to 100.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres (GMTs) for Meningococcal Serogroup C (MCC) One Month After MCC-TT or MCC-CRM Doses 1 and 2 (Part 1)

| | |
|-----------------|---|
| End point title | Geometric Mean Titres (GMTs) for Meningococcal Serogroup C (MCC) One Month After MCC-TT or MCC-CRM Doses 1 and 2 (Part 1) |
|-----------------|---|

End point description:

Anti-MCC antibody GMTs were determined 1 month after MCC-TT or MCC-CRM Doses 1 and 2 in participants also treated with V419. Serum antibody levels were assayed using the Meningo C rabbit complement serum bactericidal antibody (rSBA) assay. All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 4 and Month 5 (1 month after MCC-TT/MCC-CRM Doses 1 and 2)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|---------------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 121 | 109 | | |
| Units: Titres | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Post-MCC Dose 1 anti-MCC GMTs (n=125, 111) | 1353 (1058.4 to 1729.6) | 285.0 (201.5 to 403.1) | | |
| Post-MCC Dose 2 anti-MCC GMTs (n=125, 111) | 2024.7 (1689.8 to 2425.9) | 1077.4 (847.5 to 1369.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Response Rates for V419 Antigens One Month After V419 Dose 3 (Part 1)

| | |
|-----------------|---|
| End point title | Antibody (Ab) Response Rates for V419 Antigens One Month After V419 Dose 3 (Part 1) |
|-----------------|---|

End point description:

The percentage of participants meeting Ab response rates for V419 antigens was determined after Dose 3. Response rate criteria for Haemophilus influenza Type B (PRP); hepatitis B (HBsAg); diphtheria; tetanus; and polio types 1, 2, and 3 are shown below. The percentage of responders to pertussis (pertussis toxoid [PT]; filamentous haemagglutinin (FHA); fimbriae types 2 and 3 [FIM]; and pertactin [PRN]) was determined as 1) if pre-vaccination Ab concentration <lower limit of quantification (LLOQ) but post-vaccination Ab concentration ≥LLOQ; or 2) if pre-vaccination Ab concentration was ≥LLOQ but post-vaccination Ab concentration was ≥pre-immunization levels. Antibody titres were measured by RIA for PRP, enhanced chemiluminescence assay (ECi) for HBsAg, micrometabolic inhibition test (MIT) for diphtheria and poliovirus, and enzyme-linked immunosorbent assay (ELISA) for tetanus, PT, FHA, FIM, and PRN. Randomized, treated participants with data and no protocol violations are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 5 (1 month after V419 Dose 3)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 125 | 105 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Anti-PRP ≥0.15 µg/mL (n=93, 82) | 97.8 (92.4 to 99.7) | 100.0 (95.6 to 100.0) | | |
| 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) | 100.0 (97.1 to 100.0) | 100.0 (96.5 to 100.0) | | |
| Anti-Diphtheria ≥0.1 IU/mL (n=125, 104) | 68.0 (59.1 to 76.1) | 74.0 (64.5 to 82.1) | | |
| Anti-Tetanus ≥0.01 IU/mL (n=122, 105) | 100.0 (97.0 to 100.0) | 100.0 (96.5 to 100.0) | | |

| | | | | |
|--|-----------------------|-----------------------|--|--|
| Anti-Tetanus ≥ 0.1 IU/mL (n=122, 105) | 100.0 (97.0 to 100.0) | 100.0 (96.5 to 100.0) | | |
| Anti-PT seroresponse (n=100, 75) | 99.0 (94.6 to 100.0) | 100.0 (95.2 to 100.0) | | |
| Anti-FHA seroresponse (n=100, 74) | 91.0 (83.6 to 95.8) | 90.5 (81.5 to 96.1) | | |
| Anti-PRN seroresponse (n=100, 73) | 95.0 (88.7 to 98.4) | 90.4 (81.2 to 96.1) | | |
| Anti-FIM seroresponse (n=100, 75) | 96.0 (90.1 to 98.9) | 96.0 (88.8 to 99.2) | | |
| Anti-Polio 1 $\geq 1:8$ dil (n=114, 95) | 100.0 (96.8 to 100.0) | 100.0 (96.2 to 100.0) | | |
| Anti-Polio 2 $\geq 1:8$ dil (n=106, 89) | 100.0 (96.6 to 100.0) | 100.0 (95.9 to 100.0) | | |
| Anti-Polio 3 $\geq 1:8$ dil (n=90, 74) | 100.0 (96.0 to 100.0) | 100.0 (95.1 to 100.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Haemophilus influenza Type B (Polyribosylribitol Phosphate [PRP]) One Month After V419 Dose 3 (Part 1)

| | |
|-----------------|---|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Haemophilus influenza Type B (Polyribosylribitol Phosphate [PRP]) One Month After V419 Dose 3 (Part 1) |
|-----------------|---|

End point description:

The GMTs for PRP Ab titres were determined for each arm. Antibody titres for PRP were measured by radioimmunoassay (RIA). All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 5 (1 month after V419 Dose 3)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|--------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 82 | | |
| Units: $\mu\text{g/mL}$ | | | | |
| geometric mean (confidence interval 95%) | 6.44 (4.7 to 8.83) | 8.21 (6.08 to 11.09) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Hepatitis B Surface Antigen (HBsAg) One Month After V419 Dose 3 (Part 1)

| | |
|-----------------|--|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Hepatitis B |
|-----------------|--|

End point description:

The GMTs for HBsAg Ab titres were determined for each arm. Antibody titres for HBsAg were measured by enhanced chemiluminescence (ECi) assay. All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 5 (1 month after V419 Dose 3)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 93 | 82 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | 195.1 (150.7 to 252.7) | 247.7 (186.3 to 329.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Diptheria One Month After V419 Dose 3 (Part 1)

| | |
|-----------------|---|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Diptheria One Month After V419 Dose 3 (Part 1) |
|-----------------|---|

End point description:

The GMTs for diptheria Ab titres were determined for each arm. Antibody titres for diptheria were measured by enhanced micrometabolic inhibition test (MIT). All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 5 (1 month after V419 Dose 3)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 125 | 104 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | 0.198 (0.165 to 0.237) | 0.22 (0.181 to 0.268) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Tetanus One Month After V419 Dose 3 (Part 1)

| | |
|-----------------|---|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Tetanus One Month After V419 Dose 3 (Part 1) |
|-----------------|---|

End point description:

The GMTs for tetanus Ab titres were determined for each arm. Antibody titres for tetanus were determined with enzyme-linked immunosorbent assay (ELISA). All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 5 (1 month after V419 Dose 3)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 122 | 105 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | 1.03 (0.9 to 1.17) | 0.95 (0.82 to 1.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Pertussis Toxoid (PT) One Month After V419 Dose 3 (Part 1)

| | |
|-----------------|---|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Pertussis Toxoid (PT) One Month After V419 Dose 3 (Part 1) |
|-----------------|---|

End point description:

The GMTs for PT Ab titres were determined for each arm. Antibody titres for PT were measured with enzyme-linked immunosorbent assay (ELISA). All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 5 (1 month after V419 Dose 3)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 112 | 89 | | |
| Units: EU/mL | | | | |
| geometric mean (confidence interval 95%) | 131.5 (117.2 to 147.6) | 133.3 (118.3 to 150.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Filamentous Haemagglutinin (FHA) One Month After V419 Dose 3 (Part 1)

| | |
|-----------------|--|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Filamentous Haemagglutinin (FHA) One Month After V419 Dose 3 (Part 1) |
|-----------------|--|

End point description:

The GMTs for FHA were determined for each arm. Antibody titres for FHA were measured by enhanced chemiluminescence (ECi) assay. All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 5 (1 month after V419 Dose 3)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 112 | 88 | | |
| Units: EU/mL | | | | |
| geometric mean (confidence interval 95%) | 50.4 (44.8 to 56.6) | 50.1 (43.7 to 57.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Pertactin (PRN) One Month After V419 Dose 3 (Part 1)

| | |
|-----------------|---|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Pertactin (PRN) One Month After V419 Dose 3 (Part 1) |
|-----------------|---|

End point description:

The GMTs for PRN were determined for each arm. Antibody titres for PRN were measured by enhanced chemiluminescence (ECi) assay. All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 5 (1 month after V419 Dose 3)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 112 | 87 | | |
| Units: EU/mL | | | | |
| geometric mean (confidence interval 95%) | 90.4 (73.2 to 111.7) | 106.8 (83.7 to 136.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Fimbrae Types 2 and 3 (FIM) One Month After V419 Dose 3 (Part 1)

| | |
|--|---|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Fimbrae Types 2 and 3 (FIM) One Month After V419 Dose 3 (Part 1) |
| End point description: The GMTs for FIM were determined for each arm. Antibody titres for FIM were measured by enhanced chemiluminescence (ECi) assay. All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included. | |
| End point type | Secondary |
| End point timeframe: Month 5 (1 month after V419 Dose 3) | |

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 112 | 89 | | |
| Units: EU/mL | | | | |
| geometric mean (confidence interval 95%) | 401.7 (339.4 to 475.5) | 441.7 (363.2 to 537.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Polio Types 1, 2, and 3 One Month After V419 Dose 3 (Part 1)

| | |
|--|---|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Polio Types 1, 2, and 3 One Month After V419 Dose 3 (Part 1) |
| End point description: The GMTs for polio types 1, 2, and 3 were determined for each arm. Antibody titres for polio types 1, 2, and 3 were measured by micrometabolic inhibition test (MIT). All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included. | |
| End point type | Secondary |
| End point timeframe: Month 5 (1 month after V419 Dose 3) | |

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 114 | 95 | | |
| Units: titre (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| 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: Percentage of Participants with Anti-Meningococcal Serogroup C (anti-MCC) Antibody (Ab) Titre $\geq 1:8$ (1/dil) and Titre $\geq 1:28$ (1/dil) One Month After Anti-Haemophilus Influenzae Type B (Anti-Hib) Vaccination (Part 2)

| | |
|-----------------|---|
| End point title | Percentage of Participants with Anti-Meningococcal Serogroup C (anti-MCC) Antibody (Ab) Titre $\geq 1:8$ (1/dil) and Titre $\geq 1:28$ (1/dil) One Month After Anti-Haemophilus Influenzae Type B (Anti-Hib) Vaccination (Part 2) |
|-----------------|---|

End point description:

The percentage of participants with anti-MCC Ab titres $\geq 1:8$ (1/dil) and $\geq 1:28$ (1/dil) were determined prior to, and 1 month after, administration of the single HiB-MCC vaccine at 12 months of age. Serum Ab levels were assayed using the Meningo C rabbit complement serum bactericidal Ab (rSBA) assay. All randomized and treated participants with data available, who had no protocol violations that could interfere with results, and received all Part 1 vaccinations are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 12 and Month 13 (Prior to anti-Hib MCC and 1 month after anti-HiB MCC)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|-----------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 111 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Pre-Hib anti-MCC % titre $\geq 1:8$ (1/dil) [n=89, 94] | 83.1 (73.7 to 90.2) | 40.4 (30.4 to 51.0) | | |
| Pre-Hib anti-MCC % titre $\geq 1:28$ (1/dil) [n=89, 94] | 40.4 (30.2 to 51.4) | 16.0 (9.2 to 25.0) | | |
| Post-Hib anti-MCC % titre $\geq 1:8$ (1/dil)[n=109, 110] | 100.0 (96.7 to 100.0) | 97.3 (92.2 to 99.4) | | |

| | | | | |
|---|----------------------|---------------------|--|--|
| Post-Hib anti-MCC % titre $\geq 1:28$ (1/dil)[n=109,110] | 99.1 (95.0 to 100.0) | 95.5 (89.7 to 98.5) | | |
|---|----------------------|---------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody (Ab) Geometric Mean Titres (GMTs) for Meningococcal Serogroup C (MCC) One Month After Anti-Haemophilus Influenzae Type B (Anti-Hib) Meningococcal Serogroup C (MCC) Vaccination (Part 2)

| | |
|-----------------|---|
| End point title | Antibody (Ab) Geometric Mean Titres (GMTs) for Meningococcal Serogroup C (MCC) One Month After Anti-Haemophilus Influenzae Type B (Anti-Hib) Meningococcal Serogroup C (MCC) Vaccination (Part 2) |
|-----------------|---|

End point description:

Antibody GMTs were determined prior to, and 1 month after, administration of the single HiB-MCC vaccine at 12 months of age. Serum Ab levels were assayed using the Meningo C rabbit complement serum bactericidal Ab (rSBA) assay. All randomized and treated participants with data available, who had no protocol violations that could interfere with results, and received all Part 1 vaccinations are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 12 and Month 13 (Prior to anti-Hib MCC and 1 month after anti-Hib MCC)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|--|---------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 111 | | |
| Units: titre (1/dil) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Pre-Hib anti-MCC GMT (n=89, 94) | 50.3 (34.4 to 73.4) | 8.7 (5.9 to 12.9) | | |
| Post-Hib 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: Percentage of Participants with Anti-Polyribosylribitol Phosphate (PRP) Antibody (Ab) Titres $\geq 0.15 \mu\text{g/mL}$ and $\geq 1.0 \mu\text{g/mL}$ One Month After Anti-Haemophilus Influenzae Type B MCC Vaccination (Part 2)

| | |
|-----------------|---|
| End point title | Percentage of Participants with Anti-Polyribosylribitol Phosphate (PRP) Antibody (Ab) Titres $\geq 0.15 \mu\text{g/mL}$ and $\geq 1.0 \mu\text{g/mL}$ One Month After Anti-Haemophilus Influenzae Type B MCC Vaccination (Part 2) |
|-----------------|---|

End point description:

The percentage of participants with anti-PRP Ab titres ≥ 0.15 $\mu\text{g/mL}$ and ≥ 1.0 $\mu\text{g/mL}$ was determined prior to, and 1 month after, administration of the anti-Hib vaccination at Month 12. Anti-PRP Ab titres were measured with radioimmunoassay (RIA). All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 12

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|---|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 111 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Pre-Hib-MCC anti-PRP ≥ 0.15 $\mu\text{g/mL}$ (n=82, 87) | 93.9 (86.3 to 98.0) | 95.4 (88.6 to 98.7) | | |
| Pre-Hib-MCC anti-PRP ≥ 1.0 $\mu\text{g/mL}$ (n=82, 87) | 54.9 (43.5 to 65.9) | 56.3 (45.3 to 66.9) | | |
| Post-Hib-MCC anti-PRP ≥ 0.15 $\mu\text{g/mL}$ (n=110, 106) | 100.0 (96.7 to 100.0) | 100.0 (96.6 to 100.0) | | |
| Post-Hib-MCC anti-PRP ≥ 1.0 $\mu\text{g/mL}$ (n=110, 106) | 99.1 (95.0 to 100.0) | 100.0 (96.6 to 100.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titres (GMTs) for Anti-Polyribosylribitol Phosphate (PRP) Antibody (Ab) One Month After Anti-Haemophilus Influenzae Type B (HiB) MCC Vaccination (Part 2)

| | |
|-----------------|--|
| End point title | Geometric Mean Titres (GMTs) for Anti-Polyribosylribitol Phosphate (PRP) Antibody (Ab) One Month After Anti-Haemophilus Influenzae Type B (HiB) MCC Vaccination (Part 2) |
|-----------------|--|

End point description:

Anti-PRP Ab GMTs were determined prior to, and 1 month after, administration of the anti-Hib vaccination at Month 12. Anti-PRP Ab titres were measured with radioimmunoassay (RIA) and are expressed as $\mu\text{g/mL}$. All randomized and treated participants with data available and who had no protocol violations that could interfere with results are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 4 and Month 5 (1 month after MCC-TT/MCC-CRM Doses 1 and 2)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|---|--------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 111 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Pre-Hib-MCC anti-PRP ≥0.15 µg/mL (n=82, 87) | 1.09 (0.81 to 1.45) | 1.18 (0.90 to 1.55) | | |
| Post-Hib-MCC anti-PRP ≥1.0 µg/mL (n=110, 106) | 100.19 (81.05 to 123.86) | 121.00 (101.11 to 144.80) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing an Adverse Event (AE) [Part 1]

| | |
|---|--|
| End point title | Percentage of Participants Experiencing an Adverse Event (AE) [Part 1] |
| End point description: | |
| An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the investigational product, whether or not considered related to the use of the product. All randomized participants who received ≥1 dose of study medication in Part 1 are included. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 4.5 months (up to 15 days after the final Part 1 vaccination) | |

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 142 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 98.6 (95.0 to 99.8) | 97.2 (92.9 to 99.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing a Vaccine-Related Systemic Adverse Event (AE) [Part 1]

| | |
|---|--|
| End point title | Percentage of Participants Experiencing a Vaccine-Related Systemic Adverse Event (AE) [Part 1] |
| End point description: | |
| An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the investigational product, whether or not considered | |

related to the use of the product. All randomized participants who received ≥ 1 dose of study medication in Part 1 are included. As per protocol, all injection site AEs were considered vaccine-related.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to 4.5 months (up to 15 days after the final Part 1 vaccination) | |

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 142 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 98.6 (95.0 to 99.8) | 96.5 (92.0 to 98.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing a Solicited Injection Site Reaction (ISR) at the V419 Injection Site (Part 1)

| | |
|---|---|
| End point title | Percentage of Participants Experiencing a Solicited Injection Site Reaction (ISR) at the V419 Injection Site (Part 1) |
| End point description: | |
| The percentage of participants with solicited ISRs was determined for each arm. Solicited ISRs consisted of injection site pain, erythema, and swelling. All randomized participants who received ≥ 1 dose of study medication in Part 1 are included. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 4.5 months (up to 15 days after the final Part 1 vaccination) | |

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 142 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Erythema (n=142, 142) | 71.1 (62.9 to 78.4) | 64.8 (56.3 to 72.6) | | |
| Pain (n=142, 142) | 63.4 (54.9 to 71.3) | 66.2 (57.8 to 73.9) | | |
| Swelling (n=142, 142) | 51.4 (42.9 to 59.9) | 47.2 (38.8 to 55.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing an Unsolicited Injection Site Reaction (ISR) at the V419 Injection Site (Part 1)

| | |
|-----------------|--|
| End point title | Percentage of Participants Experiencing an Unsolicited Injection Site Reaction (ISR) at the V419 Injection Site (Part 1) |
|-----------------|--|

End point description:

The percentage of participants with unsolicited ISRs was determined for each arm. Unsolicited ISRs were any injection-site ISRs not considered solicited. All randomized participants who received ≥ 1 dose of study medication in Part 1 are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 4.5 months (up to 15 days after the final Part 1 vaccination)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|-----------------------------------|-------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 142 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 6.3 (2.9 to 11.7) | 11.3 (6.6 to 17.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing a Solicited Injection Site Reaction (ISR) at the MCC-TT or MCC-CRM Injection Site (Part 1)

| | |
|-----------------|--|
| End point title | Percentage of Participants Experiencing a Solicited Injection Site Reaction (ISR) at the MCC-TT or MCC-CRM Injection Site (Part 1) |
|-----------------|--|

End point description:

The percentage of participants with solicited ISRs was determined for each arm. Solicited ISRs consisted of injection site pain, erythema, and swelling. All randomized participants who received ≥ 1 dose of study medication in Part 1 are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 4.5 months (up to 15 days after the final Part 1 vaccination)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 142 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Erythema (n=142, 142) | 56.3 (47.8 to 64.6) | 45.8 (37.4 to 54.3) | | |

| | | | | |
|-----------------------|---------------------|---------------------|--|--|
| Pain (n=142, 142) | 41.5 (33.3 to 50.1) | 45.8 (37.4 to 54.3) | | |
| Swelling (n=142, 142) | 35.9 (28.0 to 44.4) | 28.2 (20.9 to 36.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing an Unsolicited Injection Site Reaction (ISR) at the MCC-TT or MCC-CRM Injection Site (Part 1)

| | |
|-----------------|---|
| End point title | Percentage of Participants Experiencing an Unsolicited Injection Site Reaction (ISR) at the MCC-TT or MCC-CRM Injection Site (Part 1) |
|-----------------|---|

End point description:

The percentage of participants with unsolicited ISRs was determined for each arm. Unsolicited ISRs consisted of bruising, dermatitis, erythema, induration, mass, pain, rash, and warmth. All randomized participants who received ≥ 1 dose of study medication in Part 1 are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 4.5 months (up to 15 days after the final Part 1 vaccination)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|-----------------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 142 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Bruising (n=142, 142) | 1.4 | 4.2 | | |
| Dermatitis (n=142, 142) | 0 | 0.7 | | |
| Erythema (n=142, 142) | 0 | 0.7 | | |
| Induration (n=142, 142) | 1.4 | 0.7 | | |
| Mass (n=142, 142) | 3.5 | 2.1 | | |
| Pain (n=142, 142) | 0 | 0.7 | | |
| Rash (n=142, 142) | 1.4 | 0.7 | | |
| Warmth (n=142, 142) | 0 | 2.1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing a Solicited Systemic Adverse Event (AE) [Part 1]

| | |
|-----------------|--|
| End point title | Percentage of Participants Experiencing a Solicited Systemic Adverse Event (AE) [Part 1] |
|-----------------|--|

End point description:

The percentage of participants with solicited systemic AEs was determined for each arm. Solicited

systemic AEs consisted of crying, decreased appetite, irritability, pyrexia, somnolence, and vomiting. All randomized participants who received ≥ 1 dose of study medication in Part 1 are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 4.5 months (up to 15 days after the final Part 1 vaccination)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|-----------------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 142 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Crying (n=142, 142) | 85.9 | 81.0 | | |
| Decreased appetite (n=142, 142) | 63.4 | 64.8 | | |
| Irritability (n=142, 142) | 88.0 | 81.0 | | |
| Pyrexia (n=142, 142) | 11.3 | 10.6 | | |
| Somnolence (n=142, 142) | 81.7 | 78.9 | | |
| Vomiting (n=142, 142) | 40.1 | 49.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Increased Temperature [Part 1]

| | |
|-----------------|--|
| End point title | Percentage of Participants Experiencing Increased Temperature [Part 1] |
|-----------------|--|

End point description:

The percentage of participants experiencing temperatures $\geq 38.0^\circ$ Celsius (C), $>38.5^\circ$ C, and $>39.5^\circ$ C following any Part 1 vaccination was determined. All randomized participants who received ≥ 1 dose of study medication in Part 1 are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 4.5 months (up to 15 days after the final Part 1 vaccination)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|------------------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 141 | 140 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| % $\geq 38.0^\circ$ C (n=141, 140) | 11.3 | 10.6 | | |
| % $>38.5^\circ$ C (n=141, 140) | 1.4 | 2.1 | | |
| % $>39.5^\circ$ C (n=141, 140) | 0.0 | 0.0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing a Serious Adverse Event (SAE) [Part 1]

| | |
|-----------------|--|
| End point title | Percentage of Participants Experiencing a Serious Adverse Event (SAE) [Part 1] |
|-----------------|--|

End point description:

An SAE is an event that results in death; is life-threatening; results in or prolongs hospitalization; is a congenital anomaly/birth defect; is a cancer; is an overdose; or is another important medical event that may jeopardize the participant. All randomized participants who received ≥ 1 dose of study medication in Part 1 are included.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 4.5 months (up to 15 days after the final Part 1 vaccination)

| End point values | V419 and MCC-TT | V419 and MCC-CRM | | |
|-----------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 142 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 4.2 (1.6 to 9.0) | 2.8 (0.8 to 7.1) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12.5 months (up to 14 days after the final dose of study medication)

Adverse event reporting additional description:

All participants who received ≥ 1 dose of study medication are included.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | V419 and MCC-TT |
|-----------------------|-----------------|

Reporting group description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-TT (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| | |
|-----------------------|------------------|
| Reporting group title | V419 and MCC-CRM |
|-----------------------|------------------|

Reporting group description:

In Part 1, participants received 3 doses of V419 (at 2, 3, and 4 months of age) and 2 doses of MCC-CRM (at 3 and 4 months of age). In Part 2, participants received a single dose of Hib-MCC at 12 months of age. As routine vaccination, participants also received 2 doses of Prevnar 13® (at 2 and 4 months of age) and 1 dose of an MMR vaccine (at 12 months of age).

| Serious adverse events | V419 and MCC-TT | V419 and MCC-CRM | |
|--|-----------------|------------------|--|
| 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 | | | |
| General disorders and administration site conditions | | | |
| Crying | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| 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 | |
| Hypothermia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| 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 | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| 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, thoracic and mediastinal disorders | | | |
| Choking | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| 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 | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| 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 | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| 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 | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| 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 | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| 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 alternative dictionary used: MedDRA 16.1 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 alternative dictionary used: MedDRA 16.1 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 alternative dictionary used: MedDRA 16.1 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 | V419 and MCC-TT | V419 and MCC-CRM | |
|---|-------------------------------|-------------------------------|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 140 / 142 (98.59%) | 137 / 142 (96.48%) | |
| Injury, poisoning and procedural complications Contusion alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 0 / 142 (0.00%) 0 | 3 / 142 (2.11%) 3 | |
| Nervous system disorders Somnolence alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 116 / 142 (81.69%) 227 | 112 / 142 (78.87%) 231 | |
| General disorders and administration site conditions | | | |

| | | |
|---|--------------------|--------------------|
| Crying | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 122 / 142 (85.92%) | 115 / 142 (80.99%) |
| occurrences (all) | 273 | 262 |
| Injection site bruising | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 4 / 142 (2.82%) | 7 / 142 (4.93%) |
| occurrences (all) | 4 | 12 |
| Injection site erythema | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 104 / 142 (73.24%) | 96 / 142 (67.61%) |
| occurrences (all) | 342 | 305 |
| Injection site mass | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 5 / 142 (3.52%) | 3 / 142 (2.11%) |
| occurrences (all) | 5 | 4 |
| Injection site pain | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 93 / 142 (65.49%) | 100 / 142 (70.42%) |
| occurrences (all) | 258 | 267 |
| Injection site swelling | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 78 / 142 (54.93%) | 70 / 142 (49.30%) |
| occurrences (all) | 211 | 177 |
| Injection site warmth | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 0 / 142 (0.00%) | 3 / 142 (2.11%) |
| occurrences (all) | 0 | 4 |
| Irritability | | |
| alternative dictionary used: MedDRA 16.1 | | |
| subjects affected / exposed | 125 / 142 (88.03%) | 115 / 142 (80.99%) |
| occurrences (all) | 301 | 286 |
| Pyrexia | | |
| alternative dictionary used: MedDRA 16.1 | | |

| | | | |
|---|-------------------------|--------------------------|--|
| subjects affected / exposed occurrences (all) | 19 / 142 (13.38%) 22 | 18 / 142 (12.68%) 23 | |
| Gastrointestinal disorders | | | |
| Constipation alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 4 / 142 (2.82%) 4 | 3 / 142 (2.11%) 5 | |
| Diarrhoea alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 11 / 142 (7.75%) 15 | 8 / 142 (5.63%) 11 | |
| Teething alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 7 / 142 (4.93%) 8 | 1 / 142 (0.70%) 1 | |
| Vomiting alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 57 / 142 (40.14%) 93 | 71 / 142 (50.00%) 112 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 12 / 142 (8.45%) 13 | 6 / 142 (4.23%) 6 | |
| Nasal congestion alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 4 / 142 (2.82%) 6 | 2 / 142 (1.41%) 2 | |
| Rhinorrhoea alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 4 / 142 (2.82%) 4 | 4 / 142 (2.82%) 4 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|--|--|--|--|
| Rash alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 8 / 142 (5.63%) 8 | 6 / 142 (4.23%) 7 | |
| Psychiatric disorders Insomnia alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 4 / 142 (2.82%) 4 | 1 / 142 (0.70%) 1 | |
| Infections and infestations Nasopharyngitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) Rhinitis alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 11 / 142 (7.75%) 12 8 / 142 (5.63%) 8 | 12 / 142 (8.45%) 14 6 / 142 (4.23%) 7 | |
| Metabolism and nutrition disorders Decreased appetite alternative dictionary used: MedDRA 16.1 subjects affected / exposed occurrences (all) | 91 / 142 (64.08%) 164 | 92 / 142 (64.79%) 167 | |

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