



Clinical trial results:

Open, randomised, controlled, multicenter Phase IIIb study to evaluate the immune response and safety, after the administration of GlaxoSmithKline Biologicals live attenuated measles mumps rubella varicella (MMRV) combination vaccine (Priorix tetra) or MMRV + conjugated meningococcal C vaccine (MenC) (Meningitec, Wyeth Vaccines) given to healthy children.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2011-001608-37 |
| Trial protocol | IT |
| Global end of trial date | 31 March 2014 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 01 April 2016 |
| First version publication date | 31 May 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 115555 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01506193 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330 |
| Public contact | Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.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 | Interim |
| Date of interim/final analysis | 17 February 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 March 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of MMRV vaccine co-administered with MenC conjugate vaccine compared to the first dose of MMRV vaccine alone with respect to anti-measles, anti-mumps, anti-rubella, and anti-varicella seroconversion rates at Day 42 after dose 1.

To demonstrate the non-inferiority of MenC conjugate vaccine coadministered with MMRV compared to MenC conjugate vaccine alone with respect to rSBA-MenC antibody seroprotection rates at Day 42 after vaccination.

Protection of trial subjects:

The subjects will be observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of anaphylaxis following the administration of vaccine(s).

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 06 February 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 | Italy: 716 |
| Worldwide total number of subjects | 716 |
| EEA total number of subjects | 716 |

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) | 716 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | MMRV + MenC Group |

Arm description:

Subjects who received MenC vaccine co-administered along with MMRV vaccine at Visit 1 (Day 0).

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | PRIORIX TETRA*SC 1FL+1F 0,5ML |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose of MMRV vaccine administered subcutaneously in the deltoid region of the left arm

| | |
|--|---|
| Investigational medicinal product name | MENINGITEC*INIET 1FL 0,5ML |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One dose of MenC vaccine administered intramuscularly in the tricep of the right arm

| | |
|------------------|------------|
| Arm title | MMRV Group |
|------------------|------------|

Arm description:

Subjects who received MMRV vaccine at Visit 1 (Day 0) and MenC vaccine at Visit 2 (Days 35-49).

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | PRIORIX TETRA*SC 1FL+1F 0,5ML |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose of MMRV vaccine administered subcutaneously in the deltoid region of the left arm

| | |
|--|---|
| Investigational medicinal product name | MENINGITEC*INIET 1FL 0,5ML |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One dose of MenC vaccine administered intramuscularly in the tricep of the right arm

| | |
|--|---|
| Arm title | MenC Group |
| Arm description: Subjects who received MenC vaccine at Visit 1 (Day 0) and MMRV vaccine at Visit 2 (Days 35-49) | |
| Arm type | Active comparator |
| Investigational medicinal product name | PRIORIX TETRA*SC 1FL+1F 0,5ML |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose of MMRV vaccine administered subcutaneously in the deltoid region of the left arm

| | |
|--|---|
| Investigational medicinal product name | MENINGITEC*INIET 1FL 0,5ML |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One dose of MenC vaccine administered intramuscularly in the tricep of the right arm

| Number of subjects in period 1 | MMRV + MenC Group | MMRV Group | MenC Group |
|---------------------------------------|-------------------|------------|------------|
| Started | 351 | 183 | 182 |
| Completed | 337 | 179 | 168 |
| Not completed | 14 | 4 | 14 |
| Consent withdrawn by subject | 5 | 1 | 8 |
| Protocol violation | 1 | - | 1 |
| Adverse event, non-fatal | - | - | 1 |
| Migrated/moved from study area | - | - | 1 |
| Lost to follow-up | 8 | 3 | 3 |

Baseline characteristics

Reporting groups

| | |
|---|-------------------|
| Reporting group title | MMRV + MenC Group |
| Reporting group description: | |
| Subjects who received MenC vaccine co-administered along with MMRV vaccine at Visit 1 (Day 0). | |
| Reporting group title | MMRV Group |
| Reporting group description: | |
| Subjects who received MMRV vaccine at Visit 1 (Day 0) and MenC vaccine at Visit 2 (Days 35-49). | |
| Reporting group title | MenC Group |
| Reporting group description: | |
| Subjects who received MenC vaccine at Visit 1 (Day 0) and MMRV vaccine at Visit 2 (Days 35-49) | |

| Reporting group values | MMRV + MenC Group | MMRV Group | MenC Group |
|---|-------------------|------------|------------|
| Number of subjects | 351 | 183 | 182 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: months | | | |
| arithmetic mean | 13.4 | 13.4 | 13.4 |
| standard deviation | ± 0.6 | ± 0.6 | ± 0.7 |
| Gender categorical Units: Subjects | | | |
| Female | 167 | 85 | 88 |
| Male | 184 | 98 | 94 |

| Reporting group values | Total | | |
|--|---------------------------------|--|--|
| Number of subjects | 716 | | |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) | 0 0 0 0 0 0 0 | | |

| | | | |
|-------------------|---|--|--|
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |

| | | | |
|--|-----|--|--|
| Age continuous Units: months arithmetic mean standard deviation | | | |
| Gender categorical Units: Subjects | | | |
| Female | 340 | | |
| Male | 376 | | |

End points

End points reporting groups

| | |
|------------------------------|---|
| Reporting group title | MMRV + MenC Group |
| Reporting group description: | Subjects who received MenC vaccine co-administered along with MMRV vaccine at Visit 1 (Day 0). |
| Reporting group title | MMRV Group |
| Reporting group description: | Subjects who received MMRV vaccine at Visit 1 (Day 0) and MenC vaccine at Visit 2 (Days 35-49). |
| Reporting group title | MenC Group |
| Reporting group description: | Subjects who received MenC vaccine at Visit 1 (Day 0) and MMRV vaccine at Visit 2 (Days 35-49) |

Primary: Number of seroconverted subjects for measles, mumps, rubella, and varicella virus

| | |
|------------------------|---|
| End point title | Number of seroconverted subjects for measles, mumps, rubella, and varicella virus ^[1] |
| End point description: | The data for this outcome measure are not posted since they are not available at the moment. This outcome measure will be updated with the data once available. The anticipated date for which is 31-December-2015. |
| End point type | Primary |
| End point timeframe: | 42 days after vaccination |

Notes:

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

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MMRV + MenC Group | MMRV Group | MenC Group | |
|-----------------------------|-------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 351 | 183 | 182 | |
| Units: Subjects | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms

| | |
|------------------------|--|
| End point title | Number of subjects reporting any and grade 3 solicited local symptoms ^[2] |
| End point description: | Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = Cried when limb is moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 20 millimeters (mm) of injection site. This outcome measure concerns subjects in MMRV + MenC Group and MMRV Group only. Subjects in MMRV Group did not receive MenC vaccine. |

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

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome measure concerns subjects in MMRV + MenC Group and MMRV Group only. Subjects in MMRV Group did not receive MenC vaccine.

| End point values | MMRV + MenC Group | MMRV Group | | |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 337 | 177 | | |
| Units: Subjects | | | | |
| Any Pain, Men C | 79 | 0 | | |
| Grade 3 Pain, Men C | 4 | 0 | | |
| Any Pain, MMRV | 78 | 31 | | |
| Grade 3 Pain, MMRV | 1 | 1 | | |
| Any Redness, Men C | 100 | 0 | | |
| Grade 3 Redness, Men C | 9 | 0 | | |
| Any Redness, MMRV | 92 | 41 | | |
| Grade 3 Redness, MMRV | 4 | 1 | | |
| Any Swelling, Men C | 68 | 0 | | |
| Grade 3 Swelling, Men C | 9 | 0 | | |
| Any Swelling, MMRV | 47 | 20 | | |
| Grade 3 Swelling, MMRV | 1 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms

| | |
|-----------------|--|
| End point title | Number of subjects reporting any, grade 3 and related solicited general symptoms |
|-----------------|--|

End point description:

Assessed solicited general symptoms were drowsiness, irritability/fussiness and loss of appetite. Any = occurrence of the symptom regardless of intensity grade or relationship to vaccination. Grade 3 symptom = symptom that prevented normal activity. Related = symptom assessed by the investigator as related to the vaccination.

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

End point timeframe:

During the 15-day (Days 0-14) post-vaccination period.

| End point values | MMRV + MenC Group | MMRV Group | MenC Group | |
|--------------------------------|-------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 336 | 177 | 171 | |
| Units: Subjects | | | | |
| Any Drowsiness | 148 | 89 | 56 | |
| Grade 3 Drowsiness | 16 | 12 | 6 | |
| Related Drowsiness | 128 | 67 | 46 | |
| Any Irritability/Fussiness | 187 | 104 | 84 | |
| Grade 3 Irritability/Fussiness | 30 | 13 | 7 | |
| Related Irritability/Fussiness | 158 | 82 | 64 | |
| Any Loss of appetite | 178 | 99 | 60 | |
| Grade 3 Loss of appetite | 25 | 12 | 5 | |
| Related Loss of appetite | 138 | 75 | 43 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms

| | |
|-----------------|--|
| End point title | Number of subjects reporting any, grade 3 and related solicited general symptoms |
|-----------------|--|

End point description:

Assessed solicited general symptoms were Parotid / salivary gland swelling and suspected signs of meningism / febrile convulsions. Any = occurrence of the symptom regardless of intensity grade or relationship to vaccination. Grade 3 parotid / salivary gland swelling = swelling with accompanying general symptoms and Related = symptom assessed by the investigator as related to the vaccination.

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

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

| End point values | MMRV + MenC Group | MMRV Group | MenC Group | |
|---|-------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 336 | 177 | 171 | |
| Units: Subjects | | | | |
| Any Parotid / salivary gland swelling | 3 | 4 | 0 | |
| Grade 3 Parotid / salivary gland swelling | 0 | 0 | 0 | |
| Related Parotid / salivary gland swelling | 3 | 3 | 0 | |
| Any Suspected signs of meningism | 1 | 0 | 1 | |
| Grade 3 Suspected signs of meningism | 0 | 0 | 0 | |
| Related Suspected signs of meningism | 1 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting fever per half degree

| | |
|--|--|
| End point title | Number of subjects reporting fever per half degree |
| End point description: Any fever = fever $\geq 38.0^{\circ}\text{C}$ on rectal setting, grade 3 fever = fever $> 39.5^{\circ}\text{C}$ and related = fever assessed by the investigator as causally related to study vaccination. | |
| End point type | Secondary |
| End point timeframe: During the 43-day (Days 0-42) post-vaccination period | |

| End point values | MMRV + MenC Group | MMRV Group | MenC Group | |
|-----------------------------|-------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 336 | 177 | 171 | |
| Units: Subjects | | | | |
| Any temperature | 159 | 86 | 46 | |
| Grade 3 temperature | 15 | 9 | 4 | |
| Related temperature | 178 | 84 | 28 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, localised and generalised rashes

| | |
|---|--|
| End point title | Number of subjects reporting any, localised and generalised rashes |
| End point description: Rash/exanthem was defined as: 1) measles/ rubella rashes (macular or maculo-papular rashes): presence of macules, discolored small patches or spots of the skin, neither elevated nor depressed below the skin's surface. 2) varicella rash (maculo-papulo-vesicular): simultaneous presence of macules, papules and vesicles raised above the skin's surface or other types of rash (heat rash, diaper rash etc.). Any rash = no lesions and grade 3 = > 150 lesions. | |
| End point type | Secondary |
| End point timeframe: Within the 43-day (Days 0-42) post-vaccination period | |

| End point values | MMRV + MenC Group | MMRV Group | MenC Group | |
|------------------------------------|-------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 337 | 177 | 171 | |
| Units: Subjects | | | | |
| Any, Localised or generalised rash | 91 | 41 | 15 | |
| Any, With fever rash | 59 | 30 | 2 | |
| Any, Varicella like rash | 6 | 1 | 1 | |

| | | | | |
|--|----|----|---|--|
| Any, Measles/Rubella like rash | 40 | 16 | 2 | |
| Any, Grade 3 rash | 2 | 1 | 2 | |
| Any, Related rash | 66 | 22 | 6 | |
| Localised, Any rash | 43 | 13 | 9 | |
| Localised, Administration site rash | 3 | 1 | 3 | |
| Localised, Other site rash | 40 | 12 | 6 | |
| Localised, With fever rash | 23 | 10 | 1 | |
| Localised, Varicella like rash | 2 | 0 | 0 | |
| Localised, Measles/Rubella like rash | 15 | 3 | 2 | |
| Localised, Grade 3 rash | 0 | 0 | 1 | |
| Localised, Related rash | 31 | 4 | 6 | |
| Generalised, Any rash | 54 | 28 | 6 | |
| Generalised, With fever rash | 38 | 20 | 1 | |
| Generalised, Varicella like rash | 4 | 1 | 1 | |
| Generalised, Measles/Rubella like rash | 25 | 13 | 0 | |
| Generalised, Grade 3 rash | 2 | 1 | 1 | |
| Generalised, Related rash | 39 | 18 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events

| | |
|-----------------|--|
| End point title | Number of subjects with any unsolicited adverse events |
|-----------------|--|

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product reported in addition to those solicited during the clinical study. Any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

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

End point timeframe:

Within 43 days (Days 0-42) after each vaccination

| End point values | MMRV + MenC Group | MMRV Group | MenC Group | |
|-----------------------------|-------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 351 | 183 | 182 | |
| Units: Subjects | | | | |
| Any AE(s) | 97 | 61 | 41 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs).

| | |
|------------------------|---|
| End point title | Number of subjects with serious adverse events (SAEs). |
| End point description: | Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. |
| End point type | Secondary |
| End point timeframe: | Throughout study period (from Day 0 to approximately Month 4) |

| End point values | MMRV + MenC Group | MMRV Group | MenC Group | |
|-----------------------------|-------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 351 | 183 | 182 | |
| Units: Subjects | | | | |
| Any SAE(s) | 6 | 4 | 2 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local & general symptoms were collected during Days 0-3 and Days 0-14 post-vaccination period, respectively. Unsolicited AEs were collected during the 43 day (Days 0-42) post each vaccination. SAEs were collected throughout the entire study period

Adverse event reporting additional description:

The number of occurrences reported for serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 17 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | MMRV + MenC Group |
|-----------------------|-------------------|

Reporting group description:

Subjects who received MenC vaccine co-administered along with MMRV vaccine at Visit 1 (Day 0).

| | |
|-----------------------|------------|
| Reporting group title | MMRV Group |
|-----------------------|------------|

Reporting group description:

Subjects who received MMRV vaccine at Visit 1 (Day 0) and MenC vaccine at Visit 2 (Days 35-49).

| | |
|-----------------------|------------|
| Reporting group title | MenC Group |
|-----------------------|------------|

Reporting group description:

Subjects who received MenC vaccine at Visit 1 (Day 0) and MMRV vaccine at Visit 2 (Days 35-49)

| Serious adverse events | MMRV + MenC Group | MMRV Group | MenC Group |
|---|-------------------|-----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 351 (1.71%) | 4 / 183 (2.19%) | 2 / 182 (1.10%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Skull fractured base | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 351 (0.28%) | 0 / 183 (0.00%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Febrile convulsion | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 351 (0.28%) | 0 / 183 (0.00%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 351 (0.28%) | 0 / 183 (0.00%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 351 (0.28%) | 0 / 183 (0.00%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspepsia alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 351 (0.28%) | 0 / 183 (0.00%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stomatitis alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 351 (0.28%) | 0 / 183 (0.00%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 351 (0.00%) | 1 / 183 (0.55%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Growth retardation alternative assessment type: Non-systematic | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 351 (0.28%) | 0 / 183 (0.00%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 351 (0.28%) | 1 / 183 (0.55%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 351 (0.00%) | 1 / 183 (0.55%) | 1 / 182 (0.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 351 (0.00%) | 1 / 183 (0.55%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis orbital | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 351 (0.00%) | 0 / 183 (0.00%) | 1 / 182 (0.55%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis adenovirus | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 351 (0.28%) | 0 / 183 (0.00%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 351 (0.00%) | 1 / 183 (0.55%) | 0 / 182 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | MMRV + MenC Group | MMRV Group | MenC Group |
|---|--------------------|--------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 220 / 351 (62.68%) | 114 / 183 (62.30%) | 84 / 182 (46.15%) |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 148 / 351 (42.17%) | 89 / 183 (48.63%) | 56 / 182 (30.77%) |
| occurrences (all) | 148 | 89 | 56 |
| General disorders and administration site conditions | | | |
| Injection site pain | | | |
| subjects affected / exposed | 92 / 351 (26.21%) | 31 / 183 (16.94%) | 0 / 182 (0.00%) |
| occurrences (all) | 92 | 31 | 0 |
| Injection site swelling | | | |
| subjects affected / exposed | 79 / 351 (22.51%) | 20 / 183 (10.93%) | 1 / 182 (0.55%) |
| occurrences (all) | 79 | 20 | 1 |
| Injection site erythema | | | |
| subjects affected / exposed | 121 / 351 (34.47%) | 41 / 183 (22.40%) | 0 / 182 (0.00%) |
| occurrences (all) | 121 | 41 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 178 / 351 (50.71%) | 99 / 183 (54.10%) | 60 / 182 (32.97%) |
| occurrences (all) | 178 | 99 | 60 |
| Irritability postvaccinal | | | |
| subjects affected / exposed | 187 / 351 (53.28%) | 104 / 183 (56.83%) | 84 / 182 (46.15%) |
| occurrences (all) | 187 | 104 | 84 |
| Pyrexia | | | |
| subjects affected / exposed | 220 / 351 (62.68%) | 114 / 183 (62.30%) | 64 / 182 (35.16%) |
| occurrences (all) | 220 | 114 | 64 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| alternative assessment type: Non-systematic | | | |

| | | | |
|---|-------------------------|-------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 11 / 351 (3.13%) 12 | 10 / 183 (5.46%) 10 | 4 / 182 (2.20%) 4 |
| Respiratory, thoracic and mediastinal disorders Cough alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 11 / 351 (3.13%) 11 | 10 / 183 (5.46%) 10 | 5 / 182 (2.75%) 5 |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 91 / 351 (25.93%) 91 | 41 / 183 (22.40%) 41 | 15 / 182 (8.24%) 15 |
| Infections and infestations Pharyngitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 16 / 351 (4.56%) 16 | 10 / 183 (5.46%) 10 | 9 / 182 (4.95%) 10 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 23 July 2012 | Rationale for amendment: The period of recruitment was extended from 3 to 6 months. Reporting of local solicited AEs and reporting of unsolicited AEs after vaccination at Visit 2 was not collected, because the vaccinations administered at Visit 2 were not considered as study vaccines. |
| 24 September 2012 | Rationale for amendment: Change made in the estimated sample size which was decreased from the initially estimated 808 subjects to 720 subjects. This change was made since the study sites were not able to recruit the initially estimated target population during the planned study period, due to the following reason: In November 2011, the Italian National Drug Agency (Agenzia Italiana del Farmaco [AIFA]) released a recommendation on the varicella vaccination strategy. The recommendation strongly discouraged the administration of measles mumps rubella varicella vaccine (MMRV) (Priorix Tetra) as the first dose and was in favour of the concomitant administration of the measles mumps rubella vaccine (MMR) and the monovalent varicella vaccine (V), due to the higher risk of febrile convulsions associated with the former. A section of paediatricians and health care providers (HCPs) prefer the MMR+V immunization strategy as compared to the MMRV immunization strategy. The recommendation had affected the recruitment rate of this study and a lower recruitment rate of subjects as compared to the recruitment rate forecasted based on the study feasibility activities (carried out before November 2011), was observed. The reduction in sample size from 808 subjects to 720 subjects was made keeping in mind that it provided sufficient power to answer the study objectives (to allow consistent comparison among the study arms), as the results of this study are of value to the countries/HCPs that plan to administer MMRV+ meningococcal C (MenC) vaccines concomitantly. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported