



Clinical trial results:

A pilot study of the impact of BCG administration on the immunogenicity of serogroup C meningococcal conjugate vaccine in healthy infants

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-003488-71 |
| Trial protocol | GB |
| Global end of trial date | 27 June 2018 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 19 April 2019 |
| First version publication date | 19 April 2019 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | OVG-2013/04 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02002156 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | University of Oxford |
| Sponsor organisation address | Oxford Vaccine Group and Jenner Institute, CCVTM, Churchill Hospital, Oxford, United Kingdom, OX3 7LE |
| Public contact | Oxford Vaccine Group, University of Oxford, 44 1865611400, andrew.pollard@paediatrics.ox.ac.uk |
| Scientific contact | Oxford Vaccine Group, University of Oxford, 44 1865611400, andrew.pollard@paediatrics.ox.ac.uk |

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? | No |

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 21 March 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 May 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 June 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To characterise the impact of BCG immunisation given at birth or 3 months of age on the initial response to infant serogroup C meningococcal vaccine (MenC).

Protection of trial subjects:

Ethical, Legal and Management Protection: Every effort was made to ensure that parents or guardians giving informed consent were able to understand fully the nature of the study including the risks, burdens, benefits and implications that taking part had for their child. The study involved the collection of blood samples that would not normally be part of routine care. In order to minimise any discomfort, local anaesthetic cream was offered to numb the skin prior to the sample being collected. The members of the study team undertaking venepuncture had specific training and experience in this technique. With the parent/guardians agreement two attempts at blood sampling were made and if unsuccessful a further visit was arranged by the study team.

Strict inclusion and exclusion criteria applied to the enrolment of each study participant.

The study complied with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so ensuring that the participant's anonymity was maintained throughout the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 November 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 28 |
| Worldwide total number of subjects | 28 |
| EEA total number of subjects | 28 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 28 |
| Infants and toddlers (28 days-23 months) | 0 |
| 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:

This study required that participants were enrolled as soon as possible after birth. Study information was provided before rather than after birth wherever practically possible, at visits to hospital and/or community-based antenatal clinics and ultrasound appointments, or sent by post.

Pre-assignment

Screening details:

No pre-screening was performed for this trial. Following consent at the first trial visit, screening was restricted to confirmation of eligibility, review of medical history and medical examination.

Period 1

| | |
|------------------------------|-------------------------------------|
| Period 1 title | Visit 1 Enrolment and Randomisation |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

The trial was not blinded after randomisation had been completed.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Group 1 |

Arm description:

BCG administered at V1

| | |
|--|-------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bacillus Calmette-Guérin (BCG) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for suspension for injection |
| Routes of administration | Intradermal use |

Dosage and administration details:

The BCG vaccine was given according to current UK guidelines. Wherever possible, BCG was administered into the left upper arm at the insertion of the deltoid muscle as detailed in these guidelines. The tip of the shoulder was avoided because of the increased risk of keloid formation at this site.

The dose administered was 0.05 mL for children under 12 months, 0.1 mL for children 12 months and older.

| | |
|------------------|---------|
| Arm title | Group 2 |
|------------------|---------|

Arm description:

BCG administered at visit 3 (3 months)

| | |
|--|-------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bacillus Calmette-Guérin (BCG) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for suspension for injection |
| Routes of administration | Intradermal use |

Dosage and administration details:

The BCG vaccine was given according to current UK guidelines. Wherever possible, BCG was administered into the left upper arm at the insertion of the deltoid muscle as detailed in these

guidelines. The tip of the shoulder was avoided because of the increased risk of keloid formation at this site.

The dose administered was 0.05 mL for children under 12 months, 0.1 mL for children 12 months and older.

| | |
|---|-----------------|
| Arm title | Group 3 |
| Arm description: | |
| Control - BCG offered at visit 7 (13 months) | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1 | Group 1 | Group 2 | Group 3 |
|---------------------------------------|---------|---------|---------|
| Started | 10 | 9 | 9 |
| Completed | 10 | 9 | 9 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Follow up visits (2-7) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Group 1 |

Arm description:

BCG administered at V1

All participants in the three groups in this trial followed the same visit schedule, part from the BCG administration date. The visit schedule was as follows:

Visit 2 and 4 (2 and 4 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 2 and 4 months.

Visit 3, 6 and 7 (3, 12 and 13 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 3, 12 and 13 months, including MenC. Collection of blood samples.

Visit 5 (5 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Collection of blood samples.

| | |
|--|-------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Bacillus Calmette-Guérin (BCG) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for suspension for injection |
| Routes of administration | Intradermal use |

Dosage and administration details:

The BCG vaccine was given according to current UK guidelines. Wherever possible, BCG was administered into the left upper arm at the insertion of the deltoid muscle as detailed in these

guidelines. The tip of the shoulder was avoided because of the increased risk of keloid formation at this site.

The dose administered was 0.05 mL for children under 12 months, 0.1 mL for children 12 months and older.

| | |
|---|-------------------------------------|
| Arm title | Group 2 |
| Arm description: BCG administered at visit 3 (3 months) All participants in the three groups in this trial followed the same visit schedule, part from the BCG administration date. The visit schedule was as follows: Visit 2 and 4(2 and 4 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 2 and 4 months. Visit 3, 6 and 7 (3, 12 and 13 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 3, 12 and 13 months, including MenC. Collection of blood samples. Visit 5 (5 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Collection of blood samples. | |
| Arm type | Experimental |
| Investigational medicinal product name | Bacillus Calmette-Guérin (BCG) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for suspension for injection |
| Routes of administration | Intradermal use |

Dosage and administration details:

The BCG vaccine was given according to current UK guidelines. Wherever possible, BCG was administered into the left upper arm at the insertion of the deltoid muscle as detailed in these guidelines. The tip of the shoulder was avoided because of the increased risk of keloid formation at this site.

The dose administered was 0.05 mL for children under 12 months, 0.1 mL for children 12 months and older.

| | |
|---|-----------------|
| Arm title | Group 3 |
| Arm description: Control - BCG offered at visit 7 (13 months) All participants in the three groups in this trial followed the same visit schedule, part from the BCG administration date. The visit schedule was as follows: Visit 2 and 4(2 and 4 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 2 and 4 months. Visit 3, 6 and 7 (3, 12 and 13 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 3, 12 and 13 months, including MenC. Collection of blood samples. Visit 5 (5 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Collection of blood samples. | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 2 | Group 1 | Group 2 | Group 3 |
|--------------------------------|---------|---------|---------|
| Started | 10 | 9 | 9 |
| Completed | 10 | 8 | 8 |
| Not completed | 0 | 1 | 1 |
| Consent withdrawn by subject | - | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|---------|
| Reporting group title | Group 1 |
| Reporting group description: BCG administered at V1 | |
| Reporting group title | Group 2 |
| Reporting group description: BCG administered at visit 3 (3 months) | |
| Reporting group title | Group 3 |
| Reporting group description: Control - BCG offered at visit 7 (13 months) | |

| Reporting group values | Group 1 | Group 2 | Group 3 |
|---|---------|---------|---------|
| Number of subjects | 10 | 9 | 9 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 10 | 9 | 9 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical Units: Subjects | | | |
| Female | 6 | 5 | 5 |
| Male | 4 | 4 | 4 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 28 | | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 28 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |

| | | | |
|--------------------|----|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 16 | | |
| Male | 12 | | |

End points

End points reporting groups

| | |
|---|------------------------------|
| Reporting group title | Group 1 |
| Reporting group description: BCG administered at V1 | |
| Reporting group title | Group 2 |
| Reporting group description: BCG administered at visit 3 (3 months) | |
| Reporting group title | Group 3 |
| Reporting group description: Control - BCG offered at visit 7 (13 months) | |
| Reporting group title | Group 1 |
| Reporting group description: BCG administered at V1 All participants in the three groups in this trial followed the same visit schedule, part from the BCG administration date. The visit schedule was as follows: Visit 2 and 4(2 and 4 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 2 and 4 months. Visit 3, 6 and 7 (3, 12 and 13 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 3, 12 and 13 months, including MenC. Collection of blood samples. Visit 5 (5 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Collection of blood samples. | |
| Reporting group title | Group 2 |
| Reporting group description: BCG administered at visit 3 (3 months) All participants in the three groups in this trial followed the same visit schedule, part from the BCG administration date. The visit schedule was as follows: Visit 2 and 4(2 and 4 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 2 and 4 months. Visit 3, 6 and 7 (3, 12 and 13 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 3, 12 and 13 months, including MenC. Collection of blood samples. Visit 5 (5 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Collection of blood samples. | |
| Reporting group title | Group 3 |
| Reporting group description: Control - BCG offered at visit 7 (13 months) All participants in the three groups in this trial followed the same visit schedule, part from the BCG administration date. The visit schedule was as follows: Visit 2 and 4(2 and 4 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 2 and 4 months. Visit 3, 6 and 7 (3, 12 and 13 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Administration of routine schedule vaccines due at 3, 12 and 13 months, including MenC. Collection of blood samples. Visit 5 (5 months): Confirmation of ongoing consent, eligibility and collection of interim medical history. Collection of blood samples. | |
| Subject analysis set title | MenC IgG (Primary Objective) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: MenC-specific IgG at 8 weeks following the dose of MenC vaccine (i.e. at 20 weeks of age if no delay in the schedule). (The log ₁₀ -transformed MenC-specific IgG was summarised by the subjects and each group at 20 weeks of age. The exponentiated differences between log ₁₀ -transformed group means was compared and presented as geometric mean ratios/titres with associated 95% confidence intervals) | |

Primary: MenC-specific IgG at 8 weeks following the dose of MenC vaccine

| | |
|-----------------|--|
| End point title | MenC-specific IgG at 8 weeks following the dose of MenC vaccine ^[1] |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

MenC-specific IgG at 8 weeks following the dose of MenC vaccine

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: All comparisons were considered exploratory and hypothesis-generating as this is an under powered study. Results were interpreted with appropriate caution due to the large degree of variation expected with small studies.

Statistical testing of hypotheses was not conducted as this is a small pilot study.

All results will be available in the trial publication which will be publicly available.

| End point values | Group 1 | Group 2 | Group 3 | Group 1 |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 9 | 9 | 9 |
| Units: Titre | 10 | 9 | 9 | 10 |

| End point values | Group 2 | Group 3 | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 8 | | |
| Units: Titre | 9 | 9 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Solicited adverse events to the trial vaccines were not collected for this trial, as all vaccines are licensed and were used in accordance with their marketing authorisation.

SAEs were collected throughout the trial period.

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

Dictionary used

| | |
|--------------------|------------|
| Dictionary name | Protocol |
| Dictionary version | Current ap |

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Solicited adverse events to the trial vaccines were not collected for this trial, as all vaccines are licensed and were used in accordance with their marketing authorisation.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 20 December 2013 | Documents were amended to make it clearer that the study invitation is only for babies who would not normally receive a BCG vaccine. We modified the recruitment text short and long, and updated the parent information booklet accordingly. A document was added to give to parents which outlines what samples are taken at each visit, for each of the three groups. Recruitment text documents were updated. |
| 24 February 2014 | Exploratory objective wording in the protocol was clarified around the analyses of monocyte and lymphocyte ratios and removal of a duplicated sentence regarding MenC SBA. A correction to the site of a vaccination was also made to the protocol. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported