Clinical trial results:
Towards improved meningococcal vaccines: a randomised, descriptive, open label study exploring the relationship between gene expression signatures with reactogenicity and immunogenicity following vaccination with serogroup B meningococcal vaccine(4CMenB)

Summary

EudraCT number	2014-000126-38
Trial protocol	GB
Global end of trial date	27 April 2018

Results information

Result version number	v1 (current)
This version publication date	18 January 2019
First version publication date	18 January 2019

Trial information

Trial identification

Sponsor protocol code	OVG2012/05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02080559
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford
Sponsor organisation address	Oxford Vaccine Group, CCVTM, Churchill Hospital, Oxford, United Kingdom, OX3 7LE
Public contact	Oxford Vaccine Group, University of Oxford, andrew.pollard@paediatrics.ox.ac.uk
Scientific contact	Oxford Vaccine Group, University of Oxford, 01865 611400, 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	20 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 April 2017
Global end of trial reached?	Yes
Global end of trial date	27 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the kinetics of global gene expression (i.e. the pattern of which genes are switched on/off) in whole blood, following vaccination with 4CMenB vaccine in healthy infants.

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	21 April 2014
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: 187
Worldwide total number of subjects	187
EEA total number of subjects	187

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)	187
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:

Healthy 8-12 week old Caucasian infants born between 37 and 42 weeks of gestation were recruited in the UK between 21st July 2014 and 27th May 2015.

Pre-assignment

Screening details:

Eligible participants were identified through the Child Health Database, GP surgeries, the OVG website, and antenatal clinics or classes and the Oxford Spires Midwifery-led unit of the John Radcliffe Hospital, Oxford. Interested parents were telephone screened against the eligibility criteria.

Period 1

Period 1 title	Visit 1 Enrolment
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:

Test group, subgroup 1
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 2

Arm description:

Test group, subgroup 2
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 3

Arm description:

Test group, subgroup 3
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Arm type	Experimental

Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 4

Arm description:

Test group, subgroup 4
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 5

Arm description:

Control group, subgroup 5
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Arm title	Group 6

Arm description:

Control group, subgroup 6
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Arm title	Group 7

Arm description:

Control group, subgroup 7
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Arm title	Group 8

Arm description:

Control group, subgroup 8
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	20	22	24
Completed	20	22	24

Number of subjects in period 1	Group 4	Group 5	Group 6
Started	28	21	23
Completed	28	21	23

Number of subjects in period 1	Group 7	Group 8
Started	21	28
Completed	21	28

Period 2	
Period 2 title	Study visit 2
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:

Test group, subgroup 1:
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2).

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 2

Arm description:

Test group, subgroup 2:
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:
0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 3

Arm description:
Test group, subgroup 3

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:
0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 4

Arm description:
Test group, subgroup 4

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2)

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:
0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 5

Arm description:
Control group, subgroup 5

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Arm title	Group 6

Arm description:
Control group, subgroup 6

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Arm title	Group 7

Arm description:
Control group, subgroup 7

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	
Arm title	Group 8

Arm description:

Control group, subgroup 8

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	

Number of subjects in period 2[1]	Group 1	Group 2	Group 3
Started	20	22	24
Completed	20	22	24

Number of subjects in period 2[1]	Group 4	Group 5	Group 6
Started	28	21	22
Completed	28	21	22

Number of subjects in period 2[1]	Group 7	Group 8
Started	20	26
Completed	20	26

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Four participants withdrew between time periods 1 and 2.

Period 3

Period 3 title	Visit 3 and 4: Primary Endpoint Baseline
Is this the baseline period?	Yes[2]
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Test group, subgroup 1
Baseline blood collected at V3.
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4

Arm type	Experimental

Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 2

Arm description:

Test group, subgroup 2
Baseline blood at visit 3
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 3

Arm description:

Test group, subgroup 3
Baseline blood at visit 4
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 4

Arm description:

Test group, subgroup 4
Baseline blood at visit 4
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 5

Arm description:

Control group, subgroup 5
Baseline blood at visit 3

Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4

Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	
Arm title	Group 6

Arm description:

Control group, subgroup 6
Baseline blood at visit 3
Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4

Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	
Arm title	Group 7

Arm description:

Control group, subgroup 7
Baseline blood at visit 4
Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4

Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	
Arm title	Group 8

Arm description:

Control group, subgroup 8
Baseline blood at visit 4
Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4

Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	

Notes:

[2] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: For this trial, the primary objective compared gene expression pre and post immunisation with the 2nd and 3rd dose of IMP.

Number of subjects in period 3[3][4]	Group 1	Group 2	Group 3
Started	19	22	24
Completed	19	22	24

Number of subjects in period 3[3][4]	Group 4	Group 5	Group 6
Started	28	21	22
Completed	28	21	22

Number of subjects in period 3[3][4]	Group 7	Group 8
Started	20	26
Completed	20	26

Notes:

[3] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The baseline for this trial was visit not the first visit. Five participants withdrew prior to the baseline visit.
[4] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: One participant withdrew between time periods 2 and 3.

Period 4

Period 4 title	Visit 5: Primary Endpoint
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:

Test group, subrgoup 1
Primary endpoint blood collected at V5 (V4+ 4 hours).

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 2

Arm description:

Test group, subgroup 2
Blood taken at V5=V4+24 hours

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 3

Arm description:

Test group, subgroup 3
Blood taken at V5=V4+72 hours

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 4
Arm description: Test group, subgroup 4 Blood taken at V5=V4+7 days	
Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details: 0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh	
Arm title	Group 5
Arm description: Control group, subgroup 5 Blood taken at V5=V4+4 hours	
Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	
Arm title	Group 6
Arm description: Control group, subgroup 6 Blood taken at V5=V4+24 hours	
Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	
Arm title	Group 7
Arm description: Control group, subgroup 7 Blood taken at V5=V4+72 hours	
Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	
Arm title	Group 8
Arm description: Control group, subgroup 8 Blood taken at V5=V4+7 days	
Arm type	Routine immunisation schedule only, no IMP
No investigational medicinal product assigned in this arm	

Number of subjects in period 4	Group 1	Group 2	Group 3
Started	19	22	24
Completed	19	22	24

Number of subjects in period 4	Group 4	Group 5	Group 6
Started	28	21	22
Completed	28	21	22

Number of subjects in period 4	Group 7	Group 8
Started	20	26
Completed	20	26

Period 5	
Period 5 title	Follow up visits (6-12)
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:

Test group, subgroup 1
Blood collected at visits 6, 9, 11 (V10 + 4 hours) and 12
Vaccination with Bexsero, Hib-MenC and PCV13 at visit 10
Vaccination with MMR at visit 12

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 2

Arm description:

Test group, subgroup 2
Blood collected at visits 6, 9, 11 (V10 + 24 hours) and 12
Vaccination with Bexsero, Hib-MenC and PCV13 at visit 10
Vaccination with MMR at visit 12

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 3

Arm description:

Test group, subgroup 3
Blood collected at visits 6, 10, 11 (V10 + 72 hours) and 12
Vaccination with Bexsero, Hib-MenC and PCV13 at visit 10
Vaccination with MMR at visit 12

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 4

Arm description:

Test group, subgroup 4
Blood collected at visits 6, 10, 11 (V10 + 7 days) and 12
Vaccination with Bexsero, Hib-MenC and PCV13 at visit 10
Vaccination with MMR at visit 12

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml 4CMenB by intra-muscular injection into the upper antero-lateral aspect of the right thigh

Arm title	Group 5

Arm description:

Control group, subgroup 5
Blood collected at visits 7, 9, 11 (V10 + 4 hours) and 12
Vaccination with Bexsero at visits 7 and 8
Vaccination with Hib-MenC and PCV13 at visit 10
Vaccination with MMR and Bexsero at visit 12

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Arm title	Group 6

Arm description:

Control group, subgroup 6
Blood collected at visits 7, 9, 11 (V10 + 24 hours) and 12
Vaccination with Bexsero at visits 7 and 8
Vaccination with Hib-MenC and PCV13 at visit 10
Vaccination with MMR and Bexsero at visit 12

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Arm title	Group 7

Arm description:

Control group, subgroup 7
Blood collected at visits 7, 10, 11 (V10 + 72 hours) and 12
Vaccination with Bexsero at visits 7 and 8
Vaccination with Hib-MenC and PCV13 at visit 10
Vaccination with MMR and Bexsero at visit 12

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Arm title	Group 8

Arm description:

Control group, subgroup 8
Blood collected at visits 7, 10, 11 (V10 + 7 days) and 12
Vaccination with Bexsero at visits 7 and 8
Vaccination with Hib-MenC and PCV13 at visit 10

Vaccination with MMR and Bexsero at visit 12

Arm type	Routine immunisation schedule only, no IMP

No investigational medicinal product assigned in this arm

Number of subjects in period 5	Group 1	Group 2	Group 3
Started	19	22	24
Completed	18	22	24
Not completed	1	0	0
Consent withdrawn by subject	1	-	-

Number of subjects in period 5	Group 4	Group 5	Group 6
Started	28	21	22
Completed	28	21	22
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 5	Group 7	Group 8
Started	20	26
Completed	20	26
Not completed	0	0
Consent withdrawn by subject	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
Test group, subgroup 1 Baseline blood collected at V3. Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4	
Reporting group title	Group 2
Reporting group description:	
Test group, subgroup 2 Baseline blood at visit 3 Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4	
Reporting group title	Group 3
Reporting group description:	
Test group, subgroup 3 Baseline blood at visit 4 Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4	
Reporting group title	Group 4
Reporting group description:	
Test group, subgroup 4 Baseline blood at visit 4 Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4	
Reporting group title	Group 5
Reporting group description:	
Control group, subgroup 5 Baseline blood at visit 3 Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4	
Reporting group title	Group 6
Reporting group description:	
Control group, subgroup 6 Baseline blood at visit 3 Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4	
Reporting group title	Group 7
Reporting group description:	
Control group, subgroup 7 Baseline blood at visit 4 Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4	
Reporting group title	Group 8
Reporting group description:	
Control group, subgroup 8 Baseline blood at visit 4 Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4	

Reporting group values	Group 1	Group 2	Group 3
Number of subjects	19	22	24

Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	19	22	24
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	7	13	10
Male	12	9	14

Reporting group values	Group 4	Group 5	Group 6
Number of subjects	28	21	22
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	28	21	22
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	14	7	12
Male	14	14	10

Reporting group values	Group 7	Group 8	Total
Number of subjects	20	26	182
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	20	26	182
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	11	9	83
Male	9	17	99

End points

End points reporting groups

Reporting group title	Group 1

Reporting group description:

Test group, subgroup 1
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Reporting group title	Group 2

Reporting group description:

Test group, subgroup 2
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Reporting group title	Group 3

Reporting group description:

Test group, subgroup 3
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Reporting group title	Group 4

Reporting group description:

Test group, subgroup 4
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Reporting group title	Group 5

Reporting group description:

Control group, subgroup 5
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Reporting group title	Group 6

Reporting group description:

Control group, subgroup 6
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Reporting group title	Group 7

Reporting group description:

Control group, subgroup 7
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Reporting group title	Group 8

Reporting group description:

Control group, subgroup 8
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).

Reporting group title	Group 1

Reporting group description:

Test group, subgroup 1:
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2).

Reporting group title	Group 2

Reporting group description:

Test group, subgroup 2:
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Reporting group title	Group 3

Reporting group description:

Test group, subgroup 3

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Reporting group title	Group 4

Reporting group description:

Test group, subgroup 4

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2)

Reporting group title	Group 5

Reporting group description:

Control group, subgroup 5

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Reporting group title	Group 6

Reporting group description:

Control group, subgroup 6

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Reporting group title	Group 7

Reporting group description:

Control group, subgroup 7

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Reporting group title	Group 8

Reporting group description:

Control group, subgroup 8

Vaccinated with Pediacel, MenC and Rotarix at 3 months of age

Reporting group title	Group 1

Reporting group description:

Test group, subgroup 1
Baseline blood collected at V3.
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4

Reporting group title	Group 2

Reporting group description:

Test group, subgroup 2
Baseline blood at visit 3
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4

Reporting group title	Group 3

Reporting group description:

Test group, subgroup 3
Baseline blood at visit 4
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4

Reporting group title	Group 4

Reporting group description:

Test group, subgroup 4
Baseline blood at visit 4
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age at visit 4

Reporting group title	Group 5

Reporting group description:

Control group, subgroup 5
Baseline blood at visit 3
Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4

Reporting group title	Group 6

Reporting group description:

Control group, subgroup 6
Baseline blood at visit 3
Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4

Reporting group title	Group 7

Reporting group description:

Control group, subgroup 7
Baseline blood at visit 4
Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4

Reporting group title	Group 8

Reporting group description:

Control group, subgroup 8
Baseline blood at visit 4
Vaccinated with Pediacel, PCV13 at 4 months of age at visit 4

Reporting group title	Group 1

Reporting group description:

Test group, subrgoup 1
Primary endpoint blood collected at V5 (V4+ 4 hours).

Reporting group title	Group 2

Reporting group description:

Test group, subgroup 2
Blood taken at V5=V4+24 hours

Reporting group title	Group 3

Reporting group description:

Test group, subgroup 3
Blood taken at V5=V4+72 hours

Reporting group title	Group 4

Reporting group description:

Test group, subgroup 4
Blood taken at V5=V4+7 days

Reporting group title	Group 5

Reporting group description:

Control group, subgroup 5
Blood taken at V5=V4+4 hours

Reporting group title	Group 6

Reporting group description:

Control group, subgroup 6
Blood taken at V5=V4+24 hours

Reporting group title	Group 7

Reporting group description:

Control group, subgroup 7
Blood taken at V5=V4+72 hours

Reporting group title	Group 8

Reporting group description:

Control group, subgroup 8
Blood taken at V5=V4+7 days

Reporting group title	Group 1

Reporting group description:

Test group, subgroup 1
Blood collected at visits 6, 9, 11 (V10 + 4 hours) and 12
Vaccination with Bexsero, Hib-MenC and PCV13 at visit 10
Vaccination with MMR at visit 12

Reporting group title	Group 2

Reporting group description:

Test group, subgroup 2
Blood collected at visits 6, 9, 11 (V10 + 24 hours) and 12
Vaccination with Bexsero, Hib-MenC and PCV13 at visit 10
Vaccination with MMR at visit 12

Reporting group title	Group 3

Reporting group description:

Test group, subgroup 3
Blood collected at visits 6, 10, 11 (V10 + 72 hours) and 12
Vaccination with Bexsero, Hib-MenC and PCV13 at visit 10
Vaccination with MMR at visit 12

Reporting group title	Group 4

Reporting group description:

Test group, subgroup 4
Blood collected at visits 6, 10, 11 (V10 + 7 days) and 12
Vaccination with Bexsero, Hib-MenC and PCV13 at visit 10
Vaccination with MMR at visit 12

Reporting group title	Group 5

Reporting group description:

Control group, subgroup 5
Blood collected at visits 7, 9, 11 (V10 + 4 hours) and 12
Vaccination with Bexsero at visits 7 and 8
Vaccination with Hib-MenC and PCV13 at visit 10
Vaccination with MMR and Bexsero at visit 12

Reporting group title	Group 6

Reporting group description:

Control group, subgroup 6
Blood collected at visits 7, 9, 11 (V10 + 24 hours) and 12
Vaccination with Bexsero at visits 7 and 8
Vaccination with Hib-MenC and PCV13 at visit 10
Vaccination with MMR and Bexsero at visit 12

Reporting group title	Group 7

Reporting group description:

Control group, subgroup 7
Blood collected at visits 7, 10, 11 (V10 + 72 hours) and 12
Vaccination with Bexsero at visits 7 and 8
Vaccination with Hib-MenC and PCV13 at visit 10
Vaccination with MMR and Bexsero at visit 12

Reporting group title	Group 8

Reporting group description:

Control group, subgroup 8
Blood collected at visits 7, 10, 11 (V10 + 7 days) and 12
Vaccination with Bexsero at visits 7 and 8
Vaccination with Hib-MenC and PCV13 at visit 10
Vaccination with MMR and Bexsero at visit 12

Primary: Gene expression post immunisation

End point title	Gene expression post immunisation[1]

End point description:

Analysis of differentially expressed genes in whole blood at 4hr, 24hr, 3d and 7d time points following the 2nd and 3rd doses of 4CMenB vaccine when given at 2, 4 and 12 months of age together with routine immunisations, or following routine immunisations alone given at equivalent time points

End point type	Primary

End point timeframe:

Gene expression 4, 24, 72 hours or 7 days post immunisation with a second dose of Bexsero was compared to expression at baseline.

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: Details of the statistical analyses performed will be available in the trial publication.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	22	24	28
Units: Gene counts per million				
number (not applicable)	19	22	24	28

End point values	Group 5	Group 6	Group 7	Group 8
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	22	20	26
Units: Gene counts per million				
number (not applicable)	21	22	20	26

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

7 days following the 2, 4, and 12 month vaccinations (V1, V4 & V10)
Prescription medications given in the 28 days that follow these time points

Adverse event reporting additional description:

The parents of participants were asked to maintain an electronic diary card detailing all (solicited and unsolicited) reactions in the 7 days following the 2, 4, and 12 month vaccinations (V1, V4 & V10), as well as prescription medications that are given in the 28 days that follow these time points.

Assessment type	Systematic

Dictionary used

Dictionary name	Protocol
Dictionary version	5.0

Reporting groups

Reporting group title	Group 1

Reporting group description:

Test group (routine immunisation schedule plus Bexsero).
Baseline blood collected at V3.
Primary endpoint blood collected at V5 (V4+ 4 hours).

Reporting group title	Group 2

Reporting group description:

Test group, subgroup 2
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2).
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age (V4).
Blood taken at V5=V4+24 hours

Reporting group title	Group 3

Reporting group description:

Test group, subgroup 3
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2).
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age (V4).
Blood taken at V5=V4+72 hours

Reporting group title	Group 4

Reporting group description:

Test group, subgroup 4
Vaccinated with 4CMenB, Pediacel, PCV13 and Rotarix at 2 months of age (V1).
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2).
Vaccinated with 4CMenB, Pediacel, PCV13 at 4 months of age (V4).
Blood taken at V5=V4+7 days

Reporting group title	Group 5

Reporting group description:

Control group, subgroup 5
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2).
Vaccinated with Pediacel, PCV13 at 4 months of age (V4).
Blood taken at V5=V4+4 hours

Reporting group title	Group 6

Reporting group description:

Control group, subgroup 6
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2).
Vaccinated with Pediacel, PCV13 at 4 months of age (V4).
Blood taken at V5=V4+24 hours

Reporting group title	Group 7

Reporting group description:

Control group, subgroup 7
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2).
Vaccinated with Pediacel, PCV13 at 4 months of age (V4).
Blood taken at V5=V4+72 hours

Reporting group title	Group 8

Reporting group description:

Control group, subgroup 8
Vaccinated with Pediacel, PCV13 and Rotarix at 2 months of age (V1).
Vaccinated with Pediacel, MenC and Rotarix at 3 months of age (V2).
Vaccinated with Pediacel, PCV13 at 4 months of age (V4).
Blood taken at V5=V4+7 days

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: Adverse event data for this trial only form part of the exploratory analysis and are therefore not included in this report.

Serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)	0 / 22 (0.00%)	2 / 24 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Sepsis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 22 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 22 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergy to animal	Additional description: Cow's milk intolerance		
subjects affected / exposed	0 / 20 (0.00%)	0 / 22 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchiolitis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 22 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Wheezing	Additional description: Respiratory distress/wheeze		
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Abscess			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 22 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 22 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 4	Group 5	Group 6
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 28 (7.14%)	0 / 21 (0.00%)	3 / 23 (13.04%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Sepsis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergy to animal	Additional description: Cow's milk intolerance		
subjects affected / exposed	1 / 28 (3.57%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Bronchiolitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 21 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing	Additional description: Respiratory distress/wheeze		
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Abscess			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 7	Group 8	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 21 (4.76%)	3 / 28 (10.71%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Sepsis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Hypothermia			

subjects affected / exposed	0 / 21 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergy to animal	Additional description: Cow's milk intolerance		
subjects affected / exposed	0 / 21 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchiolitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing	Additional description: Respiratory distress/wheeze		
subjects affected / exposed	0 / 21 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Abscess			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 20 (0.00%)	0 / 22 (0.00%)	0 / 24 (0.00%)

Non-serious adverse events	Group 4	Group 5	Group 6
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 28 (0.00%)	0 / 21 (0.00%)	0 / 23 (0.00%)

Non-serious adverse events	Group 7	Group 8	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 21 (0.00%)	0 / 28 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2015	This amendment updated the protocol as follows: 1. Addition of exploratory objective to evaluate the effect of maternal pertussis vaccine receipt on infant immunisation responses and addition of exploratory endpoint of concentration of infant pertussis antigens – in order to evaluate the effect of maternal pertussis vaccine receipt on infant immunisation responses 2. Temperature recording to be performed at 4 and 8 hours to better reflect time of maximum fever as identified on continuous monitoring on ibutton 3. Sample size adjusted due to being unable to collect enough blood samples at key time points to achieve the primary objective at the original sample size 4. Planed trial duration extended to 2 years in order to complete all analyses
21 March 2018	This amendment updated the protocol in relation to secondary and exploratory endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported