Clinical trial results:
An open label randomised controlled study to evaluate the induction of immune memory following infant vaccination with a glyco-conjugate Neisseria meningitidis serogroup C vaccine and to assess the immunological impact of administering routine infant immunisations in consistent versus alternating limbs

Summary

EudraCT number	2009-016579-31
Trial protocol	GB
Global end of trial date	13 October 2014

Results information

Result version number	v1 (current)
This version publication date	28 July 2019
First version publication date	28 July 2019
Summary attachment (see zip file)	MALTA Clinical Study Report (Malta MenC study Clinical Study Report_final_16_06_2015 (00000002).pdf)

Trial information

Trial identification

Sponsor protocol code	OVG2008/6

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01129518
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	Prof. Andrew Pollard, Oxford Vaccine Group, University of Oxford, +44 (0)1865 611400,
Scientific contact	Prof. Andrew Pollard, Oxford Vaccine Group, University of Oxford, +44 (0)1865 611400,

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	16 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to demonstrate non-inferiority of the geometric mean titres (GMTs) of meningococcal serogroup C (MenC) specific serum bactericidal antibodies, using rabbit complement (rSBA), 1 month after a 12 month dose of Hib-MenC vaccine in children receiving a single dose of MenC-CRM197vaccine at 3 months of age (single dose priming) compared with those receiving 2 doses at 3 and 4 months of age (2 dose priming). Non-inferiority of the MenC serum bactericidal antibody geometric mean titres (SBA GMTs) would imply that the reduced schedule of MenC immunisation would be a more cost effective method of providing sustained immunity against MenC disease through childhood.

Protection of trial subjects:

Vaccination was performed by a registered doctor or nurse.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 July 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 449
Country: Number of subjects enrolled	Malta: 60
Worldwide total number of subjects	509
EEA total number of subjects	509

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)	509
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:

UK - eligible participants identified through the child health computers of the Primary Care Trusts, approach parents/carers opportunistically on post-natal wards, GPs and Health Visitors.

Malta - eligible participants were identified through the Birth Register held at Mater Dei Hospital.

Pre-assignment

Screening details:

Measurement of axillary temperature together with a check of the inclusion and exclusion criteria to determine if the infant was healthy. Inclusion and exclusion criteria checked on the first visit during which enrolment and randomisation took place.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Single dose MenC-CRM 197 Group

Arm description:

Single dose MenC-CRM 197 vaccine with the following vaccination schedule:
V1 (age 6-12 weeks): PCV13 + DTaP-IPV-Hib
V2 (age 3 months): DTaP-IPV-Hib + MenC-CRM 197
V3 (age 4 months): DTaP-IPV-Hib + PCV13
V5 (age 5 months): PCV13 + Hib-MenC
V7 (age 13 months): MMR

Arm type	Active comparator
Investigational medicinal product name	MenC-CRM197 vaccine
Investigational medicinal product code	
Other name	Menjugate
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses

Arm title	Two dose MenC-CRM 197 Group

Arm description:

Two doses MenC-CRM 197 vaccine with the following vaccination schedule:
V1 (age 6-12 weeks): PCV13 + DTaP-IPV-Hib
V2 (age 3 months): DTaP-IPV-Hib + MenC-CRM 197
V3 (age 4 months): DTaP-IPV-Hib + PCV13 + MenC-CRM 197
V5 (age 5 months): PCV13 + Hib-MenC
V7 (age 13 months): MMR

Arm type	Active comparator
Investigational medicinal product name	MenC-CRM197
Investigational medicinal product code	
Other name	Menjugate
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received 2 doses of the MenC-TT vaccine in the study.

Arm title	Control Group

Arm description:

No MenC vaccine with the following vaccination schedule:
V1 (age 6-12 weeks): PCV13 + DTaP-IPV-Hib
V2 (age 3 months): DTaP-IPV-Hib
V3 (age 4 months): DTaP-IPV-Hib + PCV13
V5 (age 5 months): PCV13 + Hib-MenC
V7 (age 13 months): MMR

Arm type	Active comparator
Investigational medicinal product name	No MenC vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants did not receive a MenC vaccine in this study group

Arm title	Single dose MenC-TT Group

Arm description:

Single dose MenC-TT vaccine with the following vaccination schedule:
V1 (age 6-12 weeks): PCV13 + DTaP-IPV-Hib
V2 (age 3 months): DTaP-IPV-Hib + MenC-TT
V3 (age 4 months): DTaP-IPV-Hib + PCV13
V5 (age 5 months): PCV13 + Hib-MenC
V7 (age 13 months): MMR

Arm type	Active comparator
Investigational medicinal product name	MenC-TT
Investigational medicinal product code	
Other name	NeisVac-C
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of the MenC-TT vaccine

Number of subjects in period 1	Single dose MenC-CRM 197 Group	Two dose MenC-CRM 197 Group	Control Group
Started	165	161	66
Completed	158	153	62
Not completed	7	8	4
Moved out of area	2	2	-
Consent withdrawn by subject	4	4	4
Lost to follow-up	1	2	-

Number of subjects in period 1	Single dose MenC-TT Group

Started	117
Completed	105
Not completed	12
Moved out of area	6
Consent withdrawn by subject	4
Lost to follow-up	2

Baseline characteristics

End points

End points reporting groups

Reporting group title	Single dose MenC-CRM 197 Group

Reporting group description:

Single dose MenC-CRM 197 vaccine with the following vaccination schedule:
V1 (age 6-12 weeks): PCV13 + DTaP-IPV-Hib
V2 (age 3 months): DTaP-IPV-Hib + MenC-CRM 197
V3 (age 4 months): DTaP-IPV-Hib + PCV13
V5 (age 5 months): PCV13 + Hib-MenC
V7 (age 13 months): MMR

Reporting group title	Two dose MenC-CRM 197 Group

Reporting group description:

Two doses MenC-CRM 197 vaccine with the following vaccination schedule:
V1 (age 6-12 weeks): PCV13 + DTaP-IPV-Hib
V2 (age 3 months): DTaP-IPV-Hib + MenC-CRM 197
V3 (age 4 months): DTaP-IPV-Hib + PCV13 + MenC-CRM 197
V5 (age 5 months): PCV13 + Hib-MenC
V7 (age 13 months): MMR

Reporting group title	Control Group

Reporting group description:

No MenC vaccine with the following vaccination schedule:
V1 (age 6-12 weeks): PCV13 + DTaP-IPV-Hib
V2 (age 3 months): DTaP-IPV-Hib
V3 (age 4 months): DTaP-IPV-Hib + PCV13
V5 (age 5 months): PCV13 + Hib-MenC
V7 (age 13 months): MMR

Reporting group title	Single dose MenC-TT Group

Reporting group description:

Single dose MenC-TT vaccine with the following vaccination schedule:
V1 (age 6-12 weeks): PCV13 + DTaP-IPV-Hib
V2 (age 3 months): DTaP-IPV-Hib + MenC-TT
V3 (age 4 months): DTaP-IPV-Hib + PCV13
V5 (age 5 months): PCV13 + Hib-MenC
V7 (age 13 months): MMR

Primary: Primary Endpoint

End point title	Primary Endpoint[1]

End point description:

The difference in the MenC rSBA GMTs between the participants primed with two doses of MenC-CRM197 (Two Dose MenC Group, Group 2) and with one dose of MenC-CRM197 (Single Dose MenC-CRM197 Group, Group 1), one month following the Hib-MenC booster dose at 12 months.

End point type	Primary

End point timeframe:

One month following Hib-MenC booster at 12 months.

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: Please refer to the submitted clinical study plan for full details.

End point values	Single dose MenC-CRM 197 Group	Two dose MenC-CRM 197 Group	Control Group	Single dose MenC-TT Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	136	127	55	95
Units: Geometic mean titre (GMT)				
number (not applicable)	136	127	55	95

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All SAEs (from all sites) reported to the University of Oxford (CTRG) within one working day of discovery or notification of the event. CTRG will perform an initial check of the information and ensure that it is reviewed at the next TSG meeting.

Assessment type	Systematic

Dictionary used

Dictionary name	Protocol
Dictionary version	11

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: Please refer to the submitted clinical study plan for full details.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2010	PCV13 to replace PCV7 Menjugate Kit to replace NeisVac-C Delay criteria for vaccination
23 April 2010	Addition of new study group Addition of 24 month persistence sample
29 June 2010	Addition of new study sites, and site specific procedures. Clarification of statistical analyses, randomisation and blinding. Clarification of sample handling procedures. Clarification of concomitant vaccines permitted in the trial Addition of trial steering committee Correction of typographical error in Appendix C. Removal of repeated secondary endpoints. Addition of new objective and endpoint. Clarification of Group numbers
26 November 2010	Clarification of recruitment procedures Clarification of adverse event reporting procedures
10 March 2011	Clarification of recruitment procedures. Inclusion of Varicella Vaccine to list of non-study vaccines permitted.
03 June 2011	Inclusion of Hep A Vaccine to list of non-study vaccines permitted.
10 October 2011	Inclusion of interim analysis.
03 November 2011	Clarification of statistical analyses and inclusion of a second attempt to blood sampling if first is unsuccessful. Correction of typing errors.
01 June 2012	Re-wording of hypothesis tests.
25 September 2012	Clarification of V5 timelines and elimination criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to technical difficulties we have not been able to upload the data, please refer to the uploaded clinical study report.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28029540

http://www.ncbi.nlm.nih.gov/pubmed/25832102

http://www.ncbi.nlm.nih.gov/pubmed/25577661

http://www.ncbi.nlm.nih.gov/pubmed/25020050