Clinical trial results:
A phase III/IV randomised open-label study and comparison of the immunogenicity and safety of a single adolescent booster dose of a meningococcal group C conjugate-containing booster vaccine (Meningitec™, or Menjugate™, or NeisVac-C™, or Menitorix™), when given concurrently with an acellular pertussis-containing booster vaccine (Repevax™ or IPV-Boostrix™)

Summary

EudraCT number	2012-005273-31
Trial protocol	GB
Global end of trial date	31 March 2017

Results information

Result version number	v1 (current)
This version publication date	02 January 2019
First version publication date	02 January 2019

Trial information

Trial identification

Sponsor protocol code	HPARSRSG12/06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02526394
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Public Health England
Sponsor organisation address	Wellington House , London , United Kingdom, SE1 8UG
Public contact	Dr Elizabeth Coates , Public Health England, 01980 612922, elizabeth.coates@phe.gov.uk
Scientific contact	Dr Elizabeth Coates , Public Health England, 01980 612922, elizabeth.coates@phe.gov.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	17 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2017
Global end of trial reached?	Yes
Global end of trial date	31 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The two principal objectives are:

1. IMMUNE RESPONSES TO MENINGITIS C AND WHOOPING COUGH:
To estimate and compare the specific immune responses to concurrently administered booster vaccines against meningitis C and whooping cough in healthy adolescents.

Participants will be adolescents aged 14 to 17 years, who have completed the UK childhood schedule of meningitis C and whooping cough vaccines appropriate for their age. Each participant in the trial will receive two vaccines given concomitantly:
(a) a single dose of ONE of Meningitec™, Menjugate™, NeisVac-C™ , or Menitorix™ (meningitis C vaccines).
(b) EITHER Repevax or IPV-Boostrix (whooping cough containing vaccines).

Thus there will be eight different combinations of meningitis C and whooping cough-containing vaccines (and accordingly, eight arms/groups of study participants)

Blood levels of specific antibodies against meningitis C and whooping cough will be measured in each participant. The measurements will be taken

Protection of trial subjects:

Fieldwork undertaken by specialist vaccine research nurses trained in paediatric venepuncture techniques. Participants who were consented to provide blood samples were offered local anaesthetic cream prior to venepuncture

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 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: 388
Worldwide total number of subjects	388
EEA total number of subjects	388

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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	388
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

388 subjects randomised to receive one of two TdaP/IPV booster vaccines with a concomitant MenC containing booster vaccine . Subjects were recruited from general practices in Hertfordshire and Gloucestershire

Pre-assignment

Screening details:

Subjects screened to ensure they did not have any of the following conditions :
Any contraindications to receipt of the study vaccines and had received appropriate primary immunisation with a pertussis containing vaccine

Pre-assignment period milestones

Number of subjects started	388
Number of subjects completed	

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ARM1

Arm description:

Randomised to receive a five component acellular pertussis booster vaccine (Repevax™) (Sanofi).

Arm type	Experimental
Investigational medicinal product name	Repevax™Sanofi
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml

Arm title	ARM2

Arm description:

Randomised to receive a three component acellular pertussis booster vaccine IPV-Boostrix™) (GSK

Arm type	Experimental
Investigational medicinal product name	IPV-Boostrix™) (GSK
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml

Number of subjects in period 1	ARM1	ARM2
Started	195	193
Completed	195	193

Baseline characteristics

Reporting groups	
Reporting group title	ARM1
Reporting group description:	
Randomised to receive a five component acellular pertussis booster vaccine (Repevax™) (Sanofi).	
Reporting group title	ARM2
Reporting group description:	
Randomised to receive a three component acellular pertussis booster vaccine IPV-Boostrix™) (GSK	

Reporting group values	ARM1	ARM2	Total
Number of subjects	195	193	388
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)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	195	193	388
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	93	100	193
Male	102	93	195

End points

End points reporting groups	
Reporting group title	ARM1
Reporting group description:	
Randomised to receive a five component acellular pertussis booster vaccine (Repevax™) (Sanofi).	
Reporting group title	ARM2
Reporting group description:	
Randomised to receive a three component acellular pertussis booster vaccine IPV-Boostrix™) (GSK	

Primary: Primary immunological	
End point title	Primary immunological
End point description:	
• Percentage of subjects with serogroup C rSBA titres ≥ 8 at 3 -6 wks after vaccination	
End point type	Primary
End point timeframe:	
3 to 6 weeks after vaccination	

End point values	ARM1	ARM2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	186	190		
Units: integers	186	190		

Statistical analyses

Statistical analysis title	Pre planned Analysis

Statistical analysis description:

In brief, a per-protocol analysis will be completed for the immunogenicity data. Proportions with meningococcal serogroup C-specific rSBA titers ≥8 and ≥ 128 as well as GMTs will be calculated with 95% confidence intervals (95% CIs) within each study arm and also aggregating across the dTaP arms (after testing for an interaction at 1% level). Proportions with ≥4-fold rises in SBA from baseline and geometric mean fold rises from baseline will also be calculated with 95% CIs.

Comparison groups	ARM1 v ARM2
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	
P-value	< 5
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Vaccination to last visit for blood sampling at 3-6 weeks post vaccination	
Adverse event reporting additional description:	
All SAEs will be reported according to relevant research governance requirements.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	ARM 1
Reporting group description: -	
Reporting group title	ARM2
Reporting group description: -	

Serious adverse events	ARM 1	ARM2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 195 (0.00%)	0 / 193 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	ARM 1	ARM2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 195 (0.51%)	0 / 193 (0.00%)	
Skin and subcutaneous tissue disorders			
dermatitis			
subjects affected / exposed	1 / 195 (0.51%)	0 / 193 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 June 2013	Changes made as advised by the reviewing Research Ethics Committee, upon issuance of favourable ethical opinion. - .Participant's health diary included as an Appendix (Appendix 6) - Abbreviations in the Participant Information Sheet were expanded to full words (and in all other participant-facing documents: GP covering letters; pre-information leaflets; Assent Form; and Consent Forms). - Document dates and version numbers updated as appropriate
19 July 2013	Removal of Menjugate groups due to lack of product availability – changes throughout the document and appendices
07 August 2014	Addition of Denela 5% anaesthetic cream (Auden Mackenzie Ltd) to those which may be provided for use prior to venepuncture.
11 May 2015	Addition of Appendix 9 to document changes in response to a national policy change in meningococcal vaccination.
24 November 2015	Change of study title from A phase III/IV randomised open-label study and comparison of the immunogenicity and safety of a single adolescent booster dose of a meningococcal group C conjugate-containing booster vaccine (Meningitec™, OR NeisVac-C™ , OR Menitorix™), when given concurrently with an acellular pertussis-containing booster vaccine (Repevax™ or IPV-Boostrix™) To A phase III/IV randomised open-label study and comparison of the immunogenicity and safety of a single adolescent booster dose of a meningococcal booster vaccine (Meningitec™, OR NeisVac-C™ , OR Menitorix™ OR Neminrix™ OR Menveo™), when given concurrently with an acellular pertussis-containing booster vaccine (Repevax™ or IPV-Boostrix™) PIL and consent forms, and GP information letter – typographical error, Men ACWY is now substituted for MenC, reflecting the vaccine that will be given as previously approved by REC.

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.

Numbers recruited less than planned due to changing availability of concomitant meningococcal c containing vaccines . Power calculation redone to ensure adequate numbers in ARM1 and ARM2 given the quadrivalent ACYW vaccine concomitantly

Notes: