Clinical trial results:
A phase III randomised, open label clinical trial evaluating the immunogenicity of a 10-valent pneumococcal conjugate vaccine booster compared to the standard 13-valent pneumococcal conjugate vaccine booster given at 12 months of age to healthy children who have received the 13-valent pneumococcal conjugate vaccine at 2 and 4 months of age.

Summary

EudraCT number	2011-005102-30
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)	PCV10 Booster Clinical Study Report (PCV10_Final Study Report version 1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	OVG2011/05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01443416
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford
Sponsor organisation address	CTRG, Old Road, Oxford, United Kingdom, OX3 7LE
Public contact	Prof. Andrew Pollard, Oxford Vaccine Group, +44 01865857420, andrew.pollard@paediatrics.ox.ac.uk
Scientific contact	Prof. Andrew Pollard, Oxford Vaccine Group, +44 01865857420, 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 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 October 2014
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 assess whether the study vaccine (PHiD-CV) is as good as the standard vaccine (PCV-13) in terms of percentage of participants who have antibody concentrations above the protective threshold (≥0.35mcg/ml) for the 10 serotypes included in PHiD-CV (serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F) one month following booster vaccination at 12 months of age with PHiD-CV or PCV-13.

Protection of trial subjects:

All study procedures were performed by qualified, trained staff delegated by the PI. Standard practice equivalent to clinical care is used for vaccination and venepuncture in all paediatric studies.

All serious adverse events were reported to the sponsor, who provided safety oversight and ensured that all SAEs were reviewed by a medical monitor on a regular basis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 April 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	United Kingdom: 178
Worldwide total number of subjects	178
EEA total number of subjects	178

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)	178
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:

177 healthy children who have been vaccinated according to the routine immunisation schedule and received the 13-valent pneumococcal conjugate vaccine at 2 and 4 months of age were enrolled during a 6 month period starting in April 2012.

Pre-assignment

Screening details:

No screening visit was performed. Enrolment was performed during the first study visit at which randomisation was performed and IMP was administered.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Booster vaccination with PHiD-CV (Synflorix®, GSK Biologicals)

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

Dosage and administration details:

Administer a single 0.5-ml dose of PHiD-CV or PCV-13 via intramuscular injection into the anterolateral aspect of either thigh.

Arm title	Group 2

Arm description:

Booster vaccination with PCV-13 (Prevenar 13®, Pfizer)

Arm type	Experimental
Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Administer a single 0.5-ml dose of PHiD-CV or PCV-13 via intramuscular injection into the anterolateral aspect of either thigh. .

Number of subjects in period 1[1]	Group 1	Group 2
Started	87	90
Completed	87	90

Notes:

[1] - 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: One participant withdrew consent prior to vaccination.

Period 2

Period 2 title	Visit 2 and 3 - Follow up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 - Follow up

Arm description:

Visit 2
All participants receive routine immunisations (MMR, Hib-MenC) and blood sample collected. AE data reviewed.

Visit 3
Blood sample collected. SAE data reviewed.

Arm type	Sample collection

No investigational medicinal product assigned in this arm

Arm title	Group 2 - Follow up

Arm description:

Visit 2
All participants receive routine immunisations (MMR, Hib-MenC) and blood sample collected. AE data reviewed.

Visit 3
Blood sample collected. SAE data reviewed.

Arm type	Sample collection

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Group 1 - Follow up	Group 2 - Follow up
Started	87	90
Completed	87	84
Not completed	0	6
Consent withdrawn by subject	-	4
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
Booster vaccination with PHiD-CV (Synflorix®, GSK Biologicals)	
Reporting group title	Group 2
Reporting group description:	
Booster vaccination with PCV-13 (Prevenar 13®, Pfizer)	

Reporting group values	Group 1	Group 2	Total
Number of subjects	87	90	177
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)	87	90	177
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	41	32	73
Male	46	58	104

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description:	
Booster vaccination with PHiD-CV (Synflorix®, GSK Biologicals)	
Reporting group title	Group 2
Reporting group description:	
Booster vaccination with PCV-13 (Prevenar 13®, Pfizer)	
Reporting group title	Group 1 - Follow up
Reporting group description:	
Visit 2 All participants receive routine immunisations (MMR, Hib-MenC) and blood sample collected. AE data reviewed. Visit 3 Blood sample collected. SAE data reviewed.	
Reporting group title	Group 2 - Follow up
Reporting group description:	
Visit 2 All participants receive routine immunisations (MMR, Hib-MenC) and blood sample collected. AE data reviewed. Visit 3 Blood sample collected. SAE data reviewed.	

Primary: The proportion of participants with serotype-specific IgG concentrations ≥0.35mcg/ml to PCV-10 serotypes at 12 months of age one month following a booster with either PCV-10 or PCV-13.

End point title	The proportion of participants with serotype-specific IgG concentrations ≥0.35mcg/ml to PCV-10 serotypes at 12 months of age one month following a booster with either PCV-10 or PCV-13.[1]
End point description:	
End point type	Primary
End point timeframe:	
Visit 2. One month post booster dose.	

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: Statistical analysis is provided in the clinical study report which is attached.

End point values	Group 1 - Follow up	Group 2 - Follow up		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	74		
Units: Percentage	70	74		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs occurring in the first 4 days after booster immunisation, and all AEs resulting in an unscheduled visits to a physician or emergency department or withdrawal from the study occurring within 1 month after vaccination were collected.

Assessment type	Systematic

Dictionary used

Dictionary name	Protocol
Dictionary version	4.0

Reporting groups

Reporting group title	Group 1

Reporting group description:

Booster vaccination with PHiD-CV (Synflorix®, GSK Biologicals)

Reporting group title	Group 2

Reporting group description:

Booster vaccination with PCV-13 (Prevenar 13®, Pfizer)

Serious adverse events	Group 1	Group 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 87 (3.45%)	2 / 90 (2.22%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 87 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea and vomiting			
subjects affected / exposed	0 / 87 (0.00%)	1 / 90 (1.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Wheezing			
subjects affected / exposed	1 / 87 (1.15%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Possible sepsis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile illness			
subjects affected / exposed	1 / 87 (1.15%)	0 / 90 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 1	Group 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 87 (54.02%)	47 / 90 (52.22%)	
General disorders and administration site conditions			
Redness	Additional description: Redness at injection site		
alternative assessment type: Non-systematic			
subjects affected / exposed	47 / 87 (54.02%)	40 / 90 (44.44%)	
occurrences (all)	47	40	
Swelling	Additional description: Swelling at injection site		
alternative assessment type: Non-systematic			
subjects affected / exposed	20 / 87 (22.99%)	21 / 90 (23.33%)	
occurrences (all)	20	21	
Harness	Additional description: Hardness at injection site		
alternative assessment type: Non-systematic			
subjects affected / exposed	25 / 87 (28.74%)	27 / 90 (30.00%)	
occurrences (all)	25	27	
Pain	Additional description: Pain at injection site		
alternative assessment type: Non-systematic			
subjects affected / exposed	27 / 87 (31.03%)	25 / 90 (27.78%)	
occurrences (all)	27	25	
Irritability postvaccinal			
subjects affected / exposed	47 / 87 (54.02%)	47 / 90 (52.22%)	
occurrences (all)	47	47	

Drowsiness			
subjects affected / exposed	25 / 87 (28.74%)	26 / 90 (28.89%)	
occurrences (all)	25	26	
Loss of appetite			
subjects affected / exposed	25 / 87 (28.74%)	26 / 90 (28.89%)	
occurrences (all)	25	26	
Fever			
subjects affected / exposed	6 / 87 (6.90%)	5 / 90 (5.56%)	
occurrences (all)	6	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 May 2012	Protocol Both vaccines in the study (Prevenar13 and Synflorix) can be given in either the arms or legs, as specified in the Summary of Product Characteristics. For ease of administration in infants injection into the leg (thigh) is preferred, in practice. The change to the procotol is to clarify that the anterolateral aspect of either thigh will be used as an injection site for either of the two vaccines administered. Whether the right or left leg is used will be documented in the diary card, as is being done currently, for information of the parents. Information Booklet Clarification that anonymised participants' information will be shared, as and when required by the Sponsor's contractual agreements, with GlaxoSmithKline who manufacture the PCV10 vaccine and fund the study. Consent Form Seeking consent for the changes made to the information booklet that clarify that anonymised participants' information will be shared, as and when required by the Sponsor's contractual agreements, with GlaxoSmithKline who manufacture the PCV10 vaccine and fund the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported