Clinical trial results:
An open label single-arm study of the immunogenicity and reactogenicity of a 13-valent pneumococcal conjugate vaccine (Prevenar13®) given to children with type 1 diabetes mellitus who have not previously received a primary schedule of immunisation with pneumococcal conjugate vaccines in infancy.

Summary

EudraCT number	2013-001024-19
Trial protocol	GB
Global end of trial date	31 December 2018

Results information

Result version number	v1 (current)
This version publication date	23 June 2022
First version publication date	23 June 2022

Trial information

Trial identification

Sponsor protocol code	OVG 2013/03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01939522
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford, Research Governance, Ethics and Assurance
Sponsor organisation address	Boundary Brook House, Churchill Drive, Oxford, United Kingdom, OX3 7LA
Public contact	Dominic F Kelly Oxford Vaccine Group University of Oxford Department of Paediatrics, University of Oxford, 0044 (01865) 611400, dominic.kelly@paediatrics.ox.ac.uk
Scientific contact	Dominic F Kelly Oxford Vaccine Group University of Oxford Department of Paediatrics, University of Oxford, 0044 (01865) 611400, dominic.kelly@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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2018
Global end of trial reached?	Yes
Global end of trial date	31 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal objective of the study is to measure pneumococcal antibody concentrations in children with T1DM (6-17 years of age) at 3 months following a single dose of PCV13. As a key secondary objective we will compare the antibody concentrations in chidlren who have previously had PPS23 versus those who have not.

Protection of trial subjects:

Subjects were offered local anaesthetic cream to reduce discomfort for blood sampling where relevant as per standard clinical procedures for this group of children in clinic

Background therapy:

All children in this study were on injected insulin for treatment of type 1 diabetes mellitus

Evidence for comparator: -

Actual start date of recruitment	03 June 2013
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: 50
Worldwide total number of subjects	50
EEA total number of subjects	0

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)	11

Adolescents (12-17 years)	39
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Children aged 6-17 years of age with T1DM who are under regular out-patient review by the diabetes team of the Oxford University Hospital NHS Trust, UK and the Royal Berkshire NHS Foundation Trust, UK were approached and given information during routine clinic visits. Enrollment was undertaken between FPFV and LPLV.

Pre-assignment

Screening details:

All children of eligible age under regular out-patient review approached during clinic visits

Period 1

Period 1 title	Enrollment period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	PCV13

Arm description:

Participants who were given a single dose of PCV13

Arm type	Experimental
Investigational medicinal product name	Prevenar13
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose (0.5ml) of Prevenar13 given intramuscularly into deltoid muscle of non-dominant arm

Number of subjects in period 1	PCV13
Started	50
Completed	49
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups

Reporting group title	Enrollment period

Reporting group description:

Children aged 6-17 years of age with T1DM who are under regular out-patient review by the diabetes team of the Oxford University Hospital NHS Trust and the Royal Berkshire NHS Foundation Trust. Eligible children will have not previously received any doses of PCV (pneumococcal conjugate vaccine) but may have been immunized with PPS23 pneumococcal polysaccharide vaccine)

Reporting group values	Enrollment period	Total	
Number of subjects	50	50	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Children (6-17 years)	50	50	
Gender categorical			
Children aged 6-17 years of age with T1DM who are under regular out-patient review by the diabetes team of the Oxford University Hospital NHS Trust and the Royal Berkshire NHS Foundation Trust. Eligible children will have not previously received any doses of PCV (pneumococcal conjugate vaccine) but may have been immunised with PPS23 (pneumococcal polysaccahride vaccine)			
Units: Subjects			
Female	26	26	
Male	24	24	

Subject analysis sets

Subject analysis set title	Children 6-17 years with T1DM
Subject analysis set type	Per protocol

Subject analysis set description:

Children aged 6-17 years of age with T1DM who are under regular out-patient review by the diabetes team of the Oxford University Hospital NHS Trust and the Royal
Berkshire NHS Foundation Trust and who have not previously received any doses of PCV but may have been immunised with PPS23.

Reporting group values	Children 6-17 years with T1DM		
Number of subjects	49		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		

Newborns (0-27 days)	0		
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		
Children (6-17 years)	49		
Gender categorical			
Children aged 6-17 years of age with T1DM who are under regular out-patient review by the diabetes team of the Oxford University Hospital NHS Trust and the Royal Berkshire NHS Foundation Trust. Eligible children will have not previously received any doses of PCV (pneumococcal conjugate vaccine) but may have been immunised with PPS23 (pneumococcal polysaccahride vaccine)			
Units: Subjects			
Female	25		
Male	24		

End points

End points reporting groups

Reporting group title	PCV13
Reporting group description:	
Participants who were given a single dose of PCV13	
Subject analysis set title	Children 6-17 years with T1DM
Subject analysis set type	Per protocol
Subject analysis set description:	
Children aged 6-17 years of age with T1DM who are under regular out-patient review by the diabetes team of the Oxford University Hospital NHS Trust and the Royal Berkshire NHS Foundation Trust and who have not previously received any doses of PCV but may have been immunised with PPS23.	

Primary: Proportion of children with vaccine pneumococcal serotype-specific (SpVS) antibody concentrations >0.35mcg/ml at 3 months following a single dose of 13-valent pneumococcal conjugate vaccine (PCV13)

End point title	Proportion of children with vaccine pneumococcal serotype-specific (SpVS) antibody concentrations >0.35mcg/ml at 3 months following a single dose of 13-valent pneumococcal conjugate vaccine (PCV13)[1]
End point description:	
Proportion of children with vaccine pneumococcal serotype-specific (SpVS) antibody concentrations >0.35mcg/ml at 3 months following a single dose of 13-valent pneumococcal conjugate vaccine	
End point type	Primary
End point timeframe:	
Time-point for primary outcome 3-months post-immunisation (V2)	

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: As specified in the protocol:
The primary outcome of the proportion of children with vaccine pneumococcal serotype-specific (SpVS) antibody concentrations >0.35mcg/ml at 3
months will be descriptive data

End point values	Children 6-17 years with T1DM			
Subject group type	Subject analysis set			
Number of subjects analysed	43[2]			
Units: Number of participants				
Serotype 1	43			
Serotype 3	43			
Serotype 4	41			
Serotype 5	42			
Serotype 6A	42			
Serotype 6B	42			
Serotype 7F	43			
Serotype 9V	43			
Serotype 14	43			
Serotype 18C	43			
Serotype 19A	43			
Serotype 19F	43			
Serotype 23F	43			

Notes:
[2] - 43 participants provided blood samples at 3-months post-immunisation

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

7 days after V1 dose of PCV13

Adverse event reporting additional description:

Diary card to record solicited and unsolicited events - posted back or collected at V2 (3-months post vaccine dose)

Assessment type	Systematic

Dictionary used

Dictionary name	non-specified
Dictionary version	1.0

Reporting groups

Reporting group title	Total study population

Reporting group description: -

Serious adverse events	Total study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 49 (4.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Endoscopy	Additional description: Single participant underwent endoscopy for symptoms which preceded entry into clinical trial – this was normal. Recorded as SAE given hospital admission for procedure.		
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Overdose	Additional description: Mental health disorder resulting in multiple attendance to hospital with overdoses and drug ingestion		
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Total study population		
Total subjects affected by non-serious adverse events subjects affected / exposed	16 / 49 (32.65%)		
General disorders and administration site conditions			
Pain	Additional description: Injection site pain		
subjects affected / exposed	13 / 49 (26.53%)		
occurrences (all)	13		
Redness	Additional description: Redness around injection site		
subjects affected / exposed	6 / 49 (12.24%)		
occurrences (all)	6		
Swelling	Additional description: Injection site swelling		
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		
Lethargy	Additional description: Lethargy post-immunisation		
subjects affected / exposed	5 / 49 (10.20%)		
occurrences (all)	5		
Headache	Additional description: Headache post-immunisation		
subjects affected / exposed	4 / 49 (8.16%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2014	Addition of reminder letter and approval for contact to be made with parent(s) by telephone prior to their next appointment. Submitted 26/2/14 - unfavourable opinion 14/3/14 Resubmitted 4/4/14 with following changes 'Opt-in' form changed to 'reply form' with the added option not to be contacted. Amendment to invitation letter to make it clear that those approached can use the telephone number on the reply slip if interested, want more information, OR if they want to decline. Amendment to protocol to emphasise that the reply form include the option to opt-out of participation. Favourable opinion 10/4/14
26 June 2015	Submitted 15/6/15 Addition of Royal Berkshire Hospital as a recruiting site. Amendment to the protocol to reflect addition of Royal Berkshire hospital as a recruiting site. The patient and parent information sheets were changed to be generic for use at both sites. Changes to how participant can return the diary card.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported