Clinical trial results:
A phase III/IV open-label study of the immunogenicity and safety of a single dose of a Live Attenuated Influenza Vaccine (LAIV) (FluenzTM) for each of three successive years in children naïve to, or in previous receipt of the AS03B adjuvanted H1N1 (2009) influenza vaccine (Pandemrix ™).

Summary

EudraCT number	2013-003592-35
Trial protocol	GB
Global end of trial date	31 March 2017

Results information

Result version number	v1 (current)
This version publication date	07 February 2019
First version publication date	07 February 2019
Summary attachment (see zip file)	Responses to live attenduated flu vaccine in children vaccinated previously with Pandremix (Responses to live attenduated flu vaccine in children vaccinated previously with Pandremix.pdf)

Trial information

Trial identification

Sponsor protocol code	LAIV Immuno

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02143882
WHO universal trial number (UTN)	-
Other trial identifiers	LAIV IMMUNO: LAIN IMMUNO

Notes:

Sponsors

Sponsor organisation name	Public Health England
Sponsor organisation address	Wellington House , London , United Kingdom, SE1 8UG
Public contact	Elizabeth Coates elizabeth.coates@phe.gov.uk, Public Health England Wellington House, London SE1 8UG, +44 0208 327 6084, elizabeth.coates@phe.gov.uk
Scientific contact	Elizabeth Coates elizabeth.coates@phe.gov.uk, Public Health England Wellington House, London SE1 8UG, +44 0208 327 6084, 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	31 March 2017
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:

Technical version:
To compare the immune response to homologous and heterologous strains before and after to annual doses of LAIV over three consecutive years in children aged 4-9(+364days) years at enrollment in naïve children vs those in previous receipt of the AS03B adjuvanted pandemic influenza vaccine to homologous vaccine strains .

Lay version:
To compare the immune system responses to various strains of flu after having the nasal influenza vaccine (LAIV) for each of three consecutive years in children aged 4-8 when they join the study and who have either previously had a dose of Pandemirix (a pandemic flu vaccine) or have never had any pandemic flu vaccine.

Protection of trial subjects:

Parents will remain at the study visit location for at least 10 minutes after vaccination to be observed by the VRN for any immediate reactions.
Reactogenicity and short term safety will be assessed in several ways.
Parents/guardians will be instructed to inform the VRN if their child is unwell or if they visit a GP or the hospital during the study duration. Health diaries will be completed from the day of vaccination until seven days after vaccination. Staff will engage in active surveillance of study participants through a telephone interview on day 8 following immunisation. On day 21 staff will collect the health diary and make further enquiry about the child's health. GPs will be asked to let the VRN know if the child becomes ill or needs care by the GP or hospital.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 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: 254
Worldwide total number of subjects	254
EEA total number of subjects	254

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)	254
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 UK children (age range 4-9 years) who have previously received Pandremix vaccine or who are naive to pandemic influenza vaccine, who are eligible to receive LAIV.

Pre-assignment

Screening details:

Healthy UK children (age range 4-9 years) who have previously received Pandremix vaccine or who are naive to pandemic influenza vaccine, who are eligible to receive LAIV.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ARM1

Arm description:

Previously vaccinated with pandemrix

Arm type	Experimental
Investigational medicinal product name	LAIV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

0.2ml

Arm title	ARM2

Arm description:

Naiive to pandemrix

Arm type	Experimental
Investigational medicinal product name	LAIV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, liquid
Routes of administration	Inhalation use

Dosage and administration details:

0.2ml

Number of subjects in period 1	ARM1	ARM2
Started	97	157
Completed	97	157

Baseline characteristics

Reporting groups	
Reporting group title	ARM1
Reporting group description:	
Previously vaccinated with pandemrix	
Reporting group title	ARM2
Reporting group description:	
Naiive to pandemrix	

Reporting group values	ARM1	ARM2	Total
Number of subjects	97	157	254
Age categorical			
Age range			
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)	97	157	254
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
LAIV and Pandremix	0	0	0
LAIV and Naive	0	0	0
Gender categorical			
Units: Subjects			
Female	46	84	130
Male	51	73	124

End points

End points reporting groups	
Reporting group title	ARM1
Reporting group description: Previously vaccinated with pandemrix	
Reporting group title	ARM2
Reporting group description: Naiive to pandemrix	

Primary: Proportion seroconverting to H1N1	
End point title	Proportion seroconverting to H1N1
End point description:	
End point type	Primary
End point timeframe: Within three weeks of vaccination	

End point values	ARM1	ARM2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	157		
Units: Percentage	2	2		

Statistical analyses

Statistical analysis title	Pre planned
Comparison groups	ARM1 v ARM2
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Fisher exact

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Between recruitment and three weeks after last dose	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	ARM1
Reporting group description: -	
Reporting group title	ARM2
Reporting group description: -	

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: This was an immunogenicity study and not a reactogenicity study.

Serious adverse events	ARM1	ARM2	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 97 (1.03%)	0 / 157 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Infection			
subjects affected / exposed	1 / 97 (1.03%)	0 / 157 (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: 5 %

Non-serious adverse events	ARM1	ARM2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 97 (0.00%)	0 / 157 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2014	Staff changes: . Methodology changes: Addition of assessment of cell mediated immune (CMI) responses through collection of a further 5ml of blood from up to 100 in each group of 9 and 10 year olds – information added in background, summary, objectives, testing of samples and in the patient information sheet and consent form. References: Addition of three extra references with regard to the addition of the CMI work.
08 December 2014	Addition of nasal swabs in the event of influenza symptoms in children enrolled in the Sniffle2 study (REC ref 14/WM/0159, NRES Committee West Midlands --Edgbaston)
22 May 2015	Extension of recruitment period into year 2 of the study due to late availability of vaccine in year 1 meaning target of 500 not reached. Planned end date of study remains unchanged i.e. year 2 recruits only participate for two years. This amendment therefore contains amended patient leaflets and consent forms for this purpose. For existing participants in the main study a letter of thanks and a study update is included. All participants in Herts aged 9 years or over in years 2 and 3 will be invited to participate in the optional CMI testing using previously approved information and consent forms. Wording has been updated to reflect this.
21 July 2015	Addition of nasal swabs in any children living in the same house as the vaccinated child in the event of influenza like illness (ILI).
18 August 2015	Addition of one box on the consent form for sibling swabbing to say the parent will only proceed if the child agrees at the time of the swab.
08 January 2016	Addition of the option of home visits
12 August 2016	Amendment of the schedule for collection of nose swabs for the third year of the study (autumn 2016 – Spring 2017) from whenever children have flu like symptoms to the days following vaccination – up to three swabs in the following week.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported