ISRCTN11725083 https://doi.org/10.1186/ISRCTN11725083

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)

Submission date
17/04/2014

Registration date
17/04/2014

Last Edited
21/06/2019

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The Department of Health has recently announced the implementation of annual vaccination for all those aged 18 years and under, with a type of flu vaccine called live attenuated influenza vaccine (LAIV). This is given as a nasal spray. The programme began in the influenza season, from September 2013, with children aged 2-4 years of age, and older children being included from the influenza season of 2014. This study aims to measure immune responses to the flu vaccination over three subsequent years.

Who can participate?
The study will include 500 children aged 5-10 years at enrolment.

What does the study involve?
All children in the study will be given flu vaccine annually and followed up over three continuous influenza seasons 2013/14, 2014/15 and 2015/16. Immune responses to the flu virus type (strain) present in the vaccine and to similar strains not contained in the vaccine, will be measured using blood samples and oral fluid samples collected before and 3 weeks after each annual vaccination. Participants will also be monitored throughout each influenza season for evidence of laboratory-confirmed influenza infection and other viral infections. Nasal swabs will be obtained by parents during any episode of influenza-like illness. Parents will be asked to complete a health diary for the week following each vaccination to record how their child has been. Serious side effects will be monitored and reported throughout the study period.

What are the possible benefits and risks of participating?
The benefit of taking part will be getting the vaccine early, since it is not known when children in

this age group will be offered flu vaccine nationally. As with all vaccines there is always a risk of anaphylaxis, but this is very rare. Blood samples may cause pain and may leave a small bruise.

Where is the study run from?
Recruitment will be via GP surgeries in Hertfordshire (UK) and Gloucestershire (UK) and potentially in London (UK).

When is the study starting and how long is it expected to run for?
The study will run from September 2014 until March 2017.

Who is funding the study?
Department of Health (UK).

Who is the main contact?
Dr Jo Southern
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Contact information

Type(s)
Scientific

Contact name
Dr Jo Southern

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Additional identifiers

EudraCT/CTIS number
2013-003592-35

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
16161

Study information

Scientific Title

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)

Acronym
LAIV Immuno

Study objectives
This study seeks primarily to measure antibody responses to the LAIV vaccination over three subsequent years.
We will also be assessing how well the vaccines are tolerated.

Primary objective:
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.

Secondary objectives:
To document the incidence of laboratory confirmed influenza and other respiratory viruses in the naïve and Pandemrix™ primed children over the three seasons.
To compare the safety and tolerability of annual doses of LAIV in naïve compared to Pandemrix™ vaccinated children

Ethics approval required
Old ethics approval format

Ethics approval(s)
West London MREC; 07/04/2014; ref. 13/LO/1854

Study design
Non-randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Prevention

Participant information sheet

Health condition(s) or problem(s) studied
Topic: Children, Primary Care; Subtopic: All Diagnoses, Not Assigned; Disease: All Diseases, All Diseases

Interventions
Each participant will receive a single dose, 0.2 ml, of Fluenz each year for three years. Particulars about the vaccine can be found at http://www.medicines.org.uk/emc/medicine/25084

This will involve six blood samples, six dried blood spots (taken from the end of the blood sample needle) and six oral fluid samples before and three weeks after each vaccination each year. These samples will allow us to assess how the immune system responds to the vaccinations in terms of the antibodies that are present. Each participant will be asked to complete a health diary for the week following vaccination. They will be asked to record any symptoms, which we will elicit in line with the information in the Summary of Product Characteristics (SPC) as well as any illnesses or visits to their GP or hospital.

Intervention Type
Biological/Vaccine

Phase
Phase IV

Primary outcome measure
The measures of immunogenicity, collected for all evaluable subjects include: Geometric mean titre.

All outcomes will be measured using blood samples, nasal swabs and diaries taken during the weeks immediately following vaccination and nasal swabs if and when a child has influenza symptoms.

Secondary outcome measures
Adverse (AE) and serious adverse events (SAEs) will be monitored

Overall study start date
01/09/2014

Completion date
31/03/2017

Eligibility

Key inclusion criteria
1. Parent/legal guardian gives written informed consent for participation of their child in the study.
2. Male or female aged 4 years (+364 days) to 8 years (+364 days) on the day of consent.
3. Documented prior receipt of Pandemrix, or no evidence in the medical notes of never having had pandemic influenza vaccine
Target Gender: Male & Female; Upper Age Limit 10 years ; Lower Age Limit 5 years

Participant type(s)
Patient

Age group
Child

Lower age limit
4 Years

Upper age limit
8 Years

Sex
Both

Target number of participants
Planned Sample Size: 500; UK Sample Size: 500;

Total final enrolment
254

Key exclusion criteria
*Absolute exclusion criteria: The participant may not enter the study if ANY of the following apply: From Fluenz Summary of Product Characterstics (SPC):
1. Hypersensitivity to the active substances, to any of the excipients (e.g. gelatin; see appendix 1), to gentamicin (a possible trace residue), to eggs or to egg proteins (e.g. ovalbumin).
2. Children and adolescents who are clinically immunodeficient due to conditions or immunosuppressive therapy such as: acute and chronic leukaemias; lymphoma; symptomatic HIV infection; cellular immune deficiencies; and high-dose corticosteroids. FLUENZ is not contraindicated for use in individuals with asymptomatic HIV infection; or individuals who are receiving topical/inhaled corticosteroids or low-dose systemic corticosteroids or those receiving corticosteroids as replacement therapy, e.g. for adrenal insufficiency.
3. Children and adolescents younger than 18 years of age receiving salicylate therapy because of the association of Reye's syndrome with salicylates and wildtype influenza infection.

Study-specific exclusions:
1. Any contraindication to vaccination as specified in the Green Book Immunisation against Infectious Disease, HMSO.
2. Known bleeding diathesis (or any condition that may be associated with a prolonged bleeding time).
3. Any other significant condition or circumstance which, in the opinion of the investigator, may either put the participant at risk because of participation in the study, or may influence the result of the study, or the participants ability to participate in the study.

*Temporary Exclusion Criteria:
From the SPC:
1. The concurrent use of FLUENZ with antiviral agents that are active against influenza A and/or B viruses has not been evaluated. However, based upon the potential for influenza antiviral agents to reduce the effectiveness of FLUENZ, it is recommended not to administer the vaccine until 48 hours after the cessation of influenza antiviral therapy. Administration of influenza antiviral agents within two weeks of vaccination may affect the response of the vaccine. Because of this information in the SPC, should any child be given these medications the administration of LAIV would be delayed as specified.

Study specific:
1. Fever (sublingual temperature = 38°C)
2. Received any blood or blood products within the past 12 weeks

Date of first enrolment
01/09/2014

Date of final enrolment
31/03/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Respiratory Diseases Department, Centre for Infectious Disease Surveillance and Control (CIDSC) , 61 Colindale Avenue
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Sponsor information

Organisation
Health Protection Agency (HPA) (UK)

Sponsor details
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Sponsor type
Government

ROR
https://ror.org/03sbpja79

Funder(s)

Funder type
Government

Funder Name
Department of Health (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			21/06/2019	No	No