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Evaluation of heterosubtypic immune responses in older people

Submission date	Recruitment status	[_] Prospectively registered
23/04/2010	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/04/2010	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
20/07/2016	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
6155; G0700846

Study information

Scientific Title
Evaluation of heterosubtypic immune responses in older people before and after seasonal and pandemic influenza vaccination

Study objectives

Vaccination is the principal means of combating epidemic and pandemic influenza. As vaccines induce relatively strain-specific and short-lived antibody responses, annual immunisation with regularly updated vaccine is recommended for seasonal influenza, but would not be expected to protect against a pandemic event. In clinical trials among immunologically naïve young adults, at least two doses of conventional avian influenza H5 or H9 subunit vaccine are needed to induce moderate homologous antibody responses. However, studies including older subjects have unexpectedly found that greater than 15% and 50% of people aged over 65 years have pre-vaccination neutralising antibody to influenza H5 and H9 haemagglutinin (HA) respectively. In contrast to recipients who are antibody-negative, these subjects mount a robust antibody response to single dose H5 or H9 pandemic vaccine, more consistent with responses seen following single dose seasonal influenza vaccine suggesting that they are effectively primed to at least some strains of avian influenza. It is important to have an understanding of the basis for this as it may help steer the development of vaccines that induce broader immunity.
Immunological objectives:
1. To evaluate heterosubtypic neutralising antibody to influenza viruses in older people
2. To evaluate heterosubtypic neutralising antibody responses to human and non-human influenza viruses following seasonal influenza vaccine
3. To evaluate homologous and heterosubtypic neutralising antibody responses to human and non-human influenza viruses after MF59-adjuvanted H5N1 vaccine

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxfordshire REC A approved on the 1st July 2008 (ref: 08/H0304/51)

Study design
Non-randomised interventional prevention trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Topic: Inflammatory and Immune System, Generic Health Relevance and Cross Cutting Themes, Infection; Subtopic: Infection (all Subtopics), Inflammatory and Immune System (all Subtopics); Disease: Immunology and inflammation, Age and ageing

Interventions
Subjects will receive two doses of monovalent 7.5 microgram MF59-adjuvanted H5N1 vaccine by intramuscular injection, 3 weeks apart. Subjects will also receive 45 microgram trivalent seasonal influenza vaccine, one dose by intramuscular injection.

Intervention Type
Other

Phase
Phase I/II

Primary outcome(s)
1. Antibody titres (geometric mean titres) and mean fold rise after vaccination at visit 2, 3, 4 and 5
2. Proportion of subjects achieving seroconversion after vaccination at visits 2, 3, 4 and 5
3. Proportion of subjects achieving seroprotection (titre of ≥1:40) after vaccination at visits 2, 3, 4 and 5

Key secondary outcome(s))
1. Cell mediated responses after vaccination at visit 1, 3 and 5
2. Frequency of solicited adverse reaction reported after vaccination at visits 2, 3, 4 and 5

Completion date
01/07/2010

Eligibility

Key inclusion criteria
1. Healthy subjects aged greater than or equal to 18 years of age, either sex
2. Subjects willing to receive vaccine in the trial
3. Able to complete informed consent and attend study visits

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Receipt of another investigational agent within 4 weeks, or before completion of the safety follow-up period in another study, whichever is longer, prior to enrolment and unwilling to refuse participation in another clinical study through the end of the study
2. Subjects who experienced any acute disease or infection requiring systemic antibiotic or antiviral therapy (chronic antibiotic therapy for urinary tract prophylaxis is acceptable) within the past 7 days before Visit 1 or any visit where trial vaccination is planned
3. Subjects who experienced fever (defined as axillary temperature greater than or equal to 38.0° C) within 3 days prior to Visit 1
4. Subjects who are pregnant or breastfeeding
5. Females of childbearing potential who refuse to use an acceptable method of birth control for the duration of the study. Adequate contraception is defined as hormonal (e.g., oral, injection, transdermal patch, implant, cervical ring), barrier (e.g., condom with spermicide or diaphragm with spermicide), intrauterine device (e.g., IUD), or monogamous relationship with vasectomized

partner who has been vasectomized for 6 months or more prior to the subject's study entry
6. Subjects with any serious disease, such as:
6.1. Cancer
6.2. Autoimmune disease (including rheumatoid arthritis)
6.3. Progressive chronic pulmonary disease (stable controlled respiratory disease including asthma is allowed)
6.4. Acute or progressive hepatic disease
6.5. Acute or progressive renal disease
7. Subjects for whom elective surgery is planned during the study period
8. Subjects with bleeding diathesis
9. Subjects with hypersensitivity to eggs, chicken protein, chicken feathers, influenza viral protein, neomycin or polymyxin or any other component of the study vaccine
10. Subjects with a history of any neurological symptoms or signs, or anaphylactic shock following administration of any vaccine
11. Subjects with known or suspected impairment/alteration of immune function, for example, resulting from:
11.1. Receipt of immunosuppressive therapy (any corticosteroid therapy or cancer chemotherapy)
11.2. Receipt of immunostimulants
11.3. Receipt of parenteral immunoglobulin preparation, blood products, and/or plasma derivatives within 3 months prior to Visit 1 or planned during the full length of the study
11.4. High risk for developing an immunocompromising disease
12. Receipt of another vaccine within 3 weeks prior to Visit 1 or planned vaccination within 3 weeks following the last study vaccination
13. Subjects with a history of (or current) drug or alcohol abuse that in the investigator's opinion would interfere with safety of the subject or the evaluation of study objectives
14. Subjects with any condition, which, in the opinion of the Investigator, might interfere with the evaluation of the study objectives

Date of first enrolment
15/08/2009

Date of final enrolment
01/07/2010

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Leicester Royal Infirmary
Leicester
United Kingdom
LE1 5WW

Sponsor information

Organisation
University Hospitals of Leicester NHS Trust (UK)

ROR
https://ror.org/02fha3693

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK) (ref: G0700846)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration