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A phase I study to assess the safety and immunogenicity of new tuberculosis (TB) vaccine candidates FP85A and MVA85A, in healthy adults who have previously been immunised with Bacillus Calmette-Guerin (BCG), using a prime-boost delivery schedule

Submission date
15/12/2009

Registration date
18/12/2009

Last Edited
31/07/2013

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
MVA85A is a new vaccine being developed against tuberculosis which is designed to act as a boosting immunisation in people who have already received the Bacillus Calmette-Guerin (BCG) vaccine. MVA85A has been given to several hundred people in whom it has been safe and also able to generate a strong immune response. In this trial MVA85A was tested alongside a second new TB vaccine, FP85A, which had not been given to humans before. We wished to study the safety of FP85A alone and also the safety of using both vaccines one after the other. We also wished to study the immune response generated by these vaccines.

Who can participate?
Healthy BCG-vaccinated adult volunteers aged 18 to 50 were recruited in Oxford, UK.

What does the study involve?
Volunteers were randomly allocated into either the first group who were vaccinated with FP85A alone, the second group who were vaccinated with MVA85A followed by FP85A 28 days later, or the third group who were vaccinated with FP85A followed by MVA85A 28 days later. The dose was the same for all groups. Volunteers were followed-up for 12 months and underwent blood tests at several time-points.

What are the possible benefits and risks of participating?
There are some known side effects of MVA85A. In healthy adults, a standard dose of intradermal MVA85A causes a mild local reaction when injected into the skin. This is visible as redness and swelling of the skin at the injection site, which lasts a week or two before healing completely without a scar. Occasionally the site of injection is also tender for a few days. About half of

volunteers also get mild flu-like symptoms (headache, tiredness, aches) following vaccination with MVA85A but these are mild. It is expected that FP85A will cause a similar range of side effects. Severe allergic reactions are rare but could potentially occur with any vaccine. Blood tests are performed throughout the trial but are not usually harmful. Having blood taken may cause slight pain and occasionally bruising at the site where the needle enters. Rarely, people feel light-headed or even faint. There are no known benefits of participating in this research.

Where is the study run from?
The study was run from the University of Oxford (UK).

When is the study starting and how long is it expected to run for?
The study ran from July 2007 to February 2010.

Who is funding the study?
The Wellcome Trust (UK).

Who is the main contact?
Professor Helen McShane, Jenner Institute, University of Oxford.

Contact information

Type(s)
Scientific

Contact name
Dr Helen McShane

Contact details
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00653770

Clinical Trials Information System (CTIS)
2007-000014-37

Protocol serial number
076943; TB017

Study information

Scientific Title

The safety and immunogenicity of new tuberculosis (TB) vaccine candidates FP85A and MVA85A, in healthy adults who have previously been immunised with Bacillus Calmette-Guerin (BCG), using a prime-boost delivery schedule: a phase I open label study

Study objectives
This is a phase I study whose primary outcome is to assess the safety of a new tuberculosis (TB) vaccine, FP85A, when administered individually and sequentially with MVA85A in a prime-boost regime, to healthy volunteers, who have previously been vaccinated with Bacillus Calmette-Guerin (BCG). The secondary outcome is to assess the cellular immune response in the same population. The trial consists of 36 subjects in three groups. The first group will be vaccinated with FP85A alone, the second group will be vaccinated with MVA85A followed by FP85A 28 days later and the third group will be vaccinated with FP85A followed by MVA85A 28 days later.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Gene Therapy Advisory Committee (GTAC) approved on the 29th March 2007 (ref: GTAC 130; EudraCT No.: 2007-000014-37)

Primary study design
Interventional

Study design
Open label three arm active-controlled phase I study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Tuberculosis

Interventions
FP85A is a modified fowlpox virus expressing antigen 85A from Mycobacterium tuberculosis. MVA85A is a modified vaccinia virus Ankara expressing antigen 85A from Mycobacterium tuberculosis. Dosing is as follows:
Group 1: 1 dose of FP85A day 0
Group 2: 1 dose of MVA85A day 0; 1 dose of FP85A day 28
Group 3: 1 dose of FP85A day 0; 1 dose of MVA85A day 28
There is no control group.

Total duration of follow-up: 12 months

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)

FP85A, MVA85A

Primary outcome(s)
To assess the safety of a new tuberculosis vaccine, FP85A, when administered individually and sequentially with MVA85A in a prime-boost regime to healthy volunteers, who have previously been vaccinated with BCG. Safety is measured throughout the one year follow up period, but specifically on the following days: 2, 7, 28, 56, 84, 168 and 364. Blood for safety testing is taken at Days 7 and 28.

Key secondary outcome(s)
To assess the cellular immune response generated by FP85A, when administered individually and sequentially with MVA85A in a prime-boost regime to healthy volunteers, who have previously been vaccinated with BCG. Immunogenicity is measured throughout the one year follow up period, but specifically on the following days: 2, 7, 28, 56, 84, 168 and 364.

Completion date
01/02/2010

Eligibility

Key inclusion criteria
1. Healthy adult aged 18 to 50 years (male or female)
2. Resident in or near Oxford for the duration of the vaccination study
3. Immunisation with BCG greater than 12 months prior to enrolment in the study
4. Able and willing (in the Investigators opinions) to comply with all study requirements
5. Willing to allow the investigators to discuss the volunteer's medical history with their General Practitioner
6. Agreement to practice barrier contraception from the start of the study until 3 months after the final vaccination
7. For females, a negative pregnancy test on the day of vaccination and agreement to practice effective contraception for the entire duration of the study
8. Agreement to refrain from blood donation during the course of the study
9. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria

1. Participation in another research study involving an investigational product in the 30 days preceding enrolment, or planned use during the study period
2. Prior receipt of a recombinant MVA or fowlpox vaccine
3. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate
4. Any confirmed or suspected immunosuppressive or immunodeficient state, including human immunodeficiency virus (HIV) infection; asplenia; recurrent, severe infections and chronic (more than 14 days) immunosuppressant medication within the past 6 months (inhaled and topical steroids are allowed)
5. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine, e.g. egg products
6. Any history of anaphylaxis in reaction to vaccination
7. Close contact with fowl during the study period (e.g. chicken farming)
8. History of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ)
9. History of serious psychiatric condition
10. Any other chronic illness requiring hospital specialist supervision
11. Suspected or known current injecting drug or alcohol abuse (as defined by an alcohol intake of greater than 42 units every week)
12. Seropositive for hepatitis B surface antigen (HBsAg)
13. Seropositive for hepatitis C virus (antibodies to HCV)
14. For females, pregnancy, lactation or willingness/intention to become pregnant during the study
15. Any other significant disease, disorder or finding, which, in the opinion of the Investigators, may either put the volunteer at risk because of participation in the study, or may influence the result of the study, or the volunteer's ability to participate in the study
16. Mantoux skin test equal to or greater than 15 millimetres
17. Screening Elispot positive (greater than 17 sfc/million PBMC) in any ESAT6 peptide or CFP10 peptide pool
18. Any clinically significant abnormal finding on screening biochemistry or haematology blood tests or urinalysis

Date of first enrolment
16/07/2007

Date of final enrolment
01/02/2010

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Jenner Institute
Oxford
United Kingdom
OX3 7DQ

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
The Wellcome Trust (UK) - Senior Clinical Fellowship Grant (grant ref: 076943)

Results and Publications

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?
Results article	results	17/08/2012		Yes	No