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A phase I study evaluating the safety and immunogenicity of a new tuberculosis (TB) vaccine, MVA85A, in healthy volunteers who are infected with human immunodeficiency virus (HIV)

Submission date
14/12/2009

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 (TB) which is designed to act as a boosting immunisation in people who have already received the Bacillus Calmette-Guerin (BCG) vaccine. In clinical trials so far it has been found to be safe in healthy people previously vaccinated with BCG, and also people with latent TB infection. In this study we wished to assess the safety of MVA85A for the first time in HIV-infected adults. We also wished to study the immune response generated by the vaccine in these volunteers. This is an important group of people to study because in parts of the world where a better TB vaccine is most needed, there is a high incidence of TB, and co-infection with HIV and TB is common and devastating.

Who can participate?
HIV-infected adult volunteers aged 18 to 50 were recruited from four hospitals in southern England.

What does the study involve?
The first group received a single low-dose injection of MVA85A and the second group received a single standard dose of MVA85A. Volunteers were followed up for one year 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 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. 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 October 2006 to August 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

Clinical Trials Information System (CTIS)
2006-000076-32

ClinicalTrials.gov (NCT)
NCT00395720

Protocol serial number
076943; TB010

Study information

Scientific Title
The safety and immunogenicity of a new tuberculosis (TB) vaccine, MVA85A, in healthy volunteers who are infected with human immunodeficiency virus (HIV): an open label phase I study

Study objectives
This is an open label phase I study of the safety and immunogenicity of two doses of MVA85A in healthy subjects who are infected with human immunodeficiency virus (HIV). Volunteers will be recruited sequentially into two groups:
Group 1 (10 volunteers): vaccinated with 5 x 10^7 pfu MVA85A
Group 2 (10 volunteers): vaccinated with 1 x 10^8 pfu MVA85A

Ethics approval required
Old ethics approval format

Ethics approval(s)
Gene Therapy Advisory Committee (GTAC) approved on the 12th May 2006 (ref: GTAC 116; EudraCT No.: 2006-000076-32)

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

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Human immunodeficiency virus (HIV), tuberculosis (TB)

Interventions
MVA85A is a modified vaccinia virus Ankara expressing antigen 85A from Mycobacterium tuberculosis. Ten subjects will receive a single intradermal vaccination of 5 x 10^7 pfu (plaque forming units) of MVA85A and ten will receive a single intradermal vaccination of 1 x 10^8 pfu MVA85A. There is no control group.

Follow up is for 12 months.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
MVA85A

Primary outcome(s)
To assess the safety of a single intradermal injection of MVA85A, when administered to healthy subjects who are infected with HIV. Safety is measured throughout the one year follow up period, but specifically on the following days: 2, 7, 14, 28, 56, 84, 168 and 364. Blood for safety testing is taken at Days 7 and 28.

Key secondary outcome(s))

To assess the immunogenicity of a single intradermal injection of MVA85A, when administered to healthy subjects who are infected with HIV. Immunogenicity is measured throughout the one year follow up period, but specifically on the following days: 7, 14, 28, 56, 84, 168 and 364.

Completion date
01/08/2010

Eligibility

Key inclusion criteria
1. Healthy adults aged 18 to 55 years (both male and female)
2. Willingness to allow the investigators to discuss the volunteer's medical history with the volunteer's HIV lead physician (and GP, if appropriate)
3. HIV antibody positive; diagnosed at least 6 months previously
4. CD4 count greater than 350; nadir CD4 not less than 300
5. HIV viral load not greater than 100,000 copies per ml
6. 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. Any clinically significant abnormal finding on screening biochemistry or haematology blood tests or on urinalysis
2. Any anti-retroviral (ARV) therapy within the past 6 months
3. Any acquired immune deficiency syndrome (AIDS) defining illness
4. Chest x-ray (CXR) showing tuberculosis (TB) or evidence of other active infection
5. Prior receipt of a recombinant MVA or Fowlpox vaccine
6. Use of any investigational or non-registered drug, live vaccine or medical device other than the study vaccine within 30 days preceding dosing of study vaccine, or planned use during the study period
7. Administration of chronic (defined as more than 14 days) immunosuppressive drugs or other immune modifying drugs within six months of vaccination. (For corticosteroids, this will mean prednisolone, or equivalent, greater than or equal to 0.5 mg/kg/day. Inhaled and topical steroids are allowed.)
8. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine, e.g. egg products
9. Presence of any underlying disease that compromises the diagnosis and evaluation of

response to the vaccine (including evidence of cardiovascular disease, history of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ), history of insulin requiring diabetes mellitus, any ongoing chronic illness requiring ongoing specialist supervision (e.g., gastrointestinal), and chronic or active neurological disease)
10. History of greater than two hospitalisations for invasive bacterial infections (pneumonia, meningitis)
11. Suspected or known current drug and/or alcohol abuse (as defined by an alcohol intake of greater than 42 units a week)
12. Seropositive for hepatitis B surface antigen (HBsAg) and/or hepatitis C (antibodies to HCV)
13. Evidence of serious psychiatric condition
14. Any other on-going chronic illness requiring hospital specialist supervision
15. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate
16. Pregnant/lactating female and any female who is willing or intends to become pregnant during the study
17. Any history of anaphylaxis in reaction to vaccination
18. PI assessment of lack of willingness to participate and comply with all requirements of the protocol, or identification of any factor felt to significantly increase the participant's risk of suffering an adverse outcome

Date of first enrolment
01/10/2006

Date of final enrolment
01/08/2010

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Jenner Institute
Oxford
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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	14/11/2011		Yes	No