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# Evaluating aerosol administration of a candidate TB vaccine, MVA85A

**Submission date**
08/11/2013

**Recruitment status**
No longer recruiting

**Registration date**
08/11/2013

**Overall study status**
Completed

**Last Edited**
03/07/2019

**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
Tuberculosis (TB) remains an important global health problem. There is an urgent need for a better vaccine as the only licensed vaccine, BCG, protects against severe TB in infancy but less well against lung disease, which is how TB spreads. MVA85A is a new vaccine that improves the effect of BCG in animals. MVA85A is a viral vector vaccine, i.e. made from a weakened virus (vector, MVA) that has been altered to contain pieces of DNA from M.tb, the bacterium which causes TB (insert, 85A). To date MVA85A has been given by an injection into the skin but it is likely that giving MVA85A directly into the lungs by a mist of air (aerosol) would be better, as the route of vaccination then matches the route by which TB is caught. A problem with virally-vectored vaccines is that individuals build up immunity to the virus base (anti-vector immunity), which makes the vaccine less efficient and also not suitable for re-use (boosting). Non-human primate data has suggested that aerosolised vaccination avoids anti-vector immunity. This proposed study aims to study the effect of aerosol vaccination of MVA85A on anti-vector and insert (85A) immunity in humans.

Who can participate?
Healthy adults aged 18-65 who live near Oxford can take part in the study.

What does the study involve?
Participants are invited for a screening visit first where the study is explained in detail and a medical review undertaken to ensure volunteers are suitable to take part. Volunteers who are enrolled will be randomly allocated to one of three groups: the first group receives the vaccine through an aerosol followed by a vaccine by injection in the skin a month later. The second group gets the vaccine by injection in the skin first followed by the vaccine by aerosol a month later. The third group receives the vaccine by a skin injection twice spaced apart by a month. Regular blood tests are performed throughout the trial and a bronchoscopy is performed 1 week after each vaccination.

What are the possible benefits and risks of participating?
Not provided at time of registration.

Where is the study run from?
University of Oxford, UK.

When is the study starting and how long is it expected to run for?
The study starts in November 2013 and runs until February 2015.

Who is funding the study?
National Institute for Health Research (NIHR), UK.

Who is the main contact?
Dr Zita-Rose Manjaly Thomas
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# Contact information

### Type(s)
Scientific

### Contact name
Dr Zita-Rose Manjaly Thomas

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# Additional identifiers

### ClinicalTrials.gov (NCT)
NCT01954563

### Clinical Trials Information System (CTIS)
2013-002020-16

### Protocol serial number
15209

# Study information

### Scientific Title
A Phase I trial evaluating mucosal administration of a candidate TB vaccine, MVA85A, as a way to induce potent local cellular immune responses and avoid anti-vector immunity

### Acronym
TB035

## Study objectives
TB remains a significant global health problem. There is an urgent need for a better vaccine as the only licensed vaccine, BCG, protects against severe TB in infancy but less well against lung disease, which is how TB spreads. MVA85A is a new vaccine that improves the effect of BCG in animals. MVA85A is a viral vector vaccine, i.e. made from a weakened virus (vector, MVA) that has been altered to contain pieces of DNA from M.tb, the pathogen which causes TB (insert, 85A). To date MVA85A has been given by an injection into the skin but it is likely that delivering MVA85A directly into the lungs by a mist of air (aerosol) would be better, as the route of vaccination then matches the route by which TB is caught.

A problem with virally-vectored vaccines is that individuals build up immunity to the virus base (anti-vector immunity) which makes the vaccine less efficient and also not suitable for reuse (boosting).

Non-human primate data has suggested that aerosolised vaccination avoids anti-vector immunity. This proposed study aims to study the effect of aerosol vaccination of MVA85A on anti-vector and insert (85A) immunity in humans in a clinical trial.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
13/SC/0329; First MREC approval date 29/07/2013

## Study design
Randomised; Interventional; Design type: Not specified

## Primary study design
Interventional

## Study type(s)
Prevention

## Health condition(s) or problem(s) studied
Topic: Infection; Subtopic: Infection (all Subtopics); Disease: Infectious diseases and microbiology

## Interventions
36 volunteers are randomised into 3 groups of 12 volunteers.

1. The first group will receive 5 x 10^7 pfu dose of MVA85A administered by aerosol followed by the same dose of the same vaccine administered by intradermal injection 1 month later.
2. The second group will receive 5 x 10^7 pfu dose of MVA85A administered by intradermal injection followed by the same dose of the same vaccine administered by aerosol 1 month later.
3. The third group will receive 5 x 10^7 pfu dose of MVA85A administered by intradermal injection followed by the same dose of the same vaccine administered by intradermal injection again 1 month later

Vaccines are administered together with a paired placebo, allowing that volunteers are blinded to route and group.

## Intervention Type

Biological/Vaccine

### Phase
Phase I

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

### Primary outcome(s)
Safety of 5 x 10^7 pfu dose of MVA85A administered by aerosol and compared to the same dose administered intradermally

### Key secondary outcome(s)
1. Characterise mucosal and systemic immunogenicity of viral vector (MVA) and insert (Ag85A) by comprehensive characterisation of humoral and cellular immune responses
2. Evaluate functional relevance of anti-vector immunity induced by aerosol and systemic immunisation in MVA85A-prime followed

Outcomes will be measured on blood tests and bronchoalveolar lavage samples (lung washings).

There is a blood test at screening, day 0, day 2, day 7, day 14, day 28, day 30, day 35, day 42, day 84 and day 168, and bronchoscopies are done on day 7 and day 35. Vaccinations are on day 0 and day 28.

### Completion date
02/02/2015

## Eligibility

### Key inclusion criteria
1. Healthy adult aged 18-55 years
2. Resident in or near Oxford for the duration of the trial period
3. No relevant findings in medical history or on physical examination
4. Confirmation of prior vaccination with BCG not less than 6 months prior to projected trial vaccination date (by visible BCG scar on examination or written documentation)
5. Allow the investigators to discuss the individuals medical history with their GP
6. Use effective contraception for the duration of the trial period (females only)
7. Refrain from blood donation during the trial
8. Give written informed consent
9. Allow the Investigator to register subject details with a confidential database to prevent concurrent entry into clinical trials
10. Able and willing (in the investigators opinion) to comply with all the trial requirements

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group

Adult

## Lower age limit
18 years

## Upper age limit
55 years

## Sex
All

## Total final enrolment
36

## Key exclusion criteria
1. Any respiratory disease, including asthma
2. Current smoker
3. Clinically significant abnormality on screening chest X-ray
4. Clinically significant abnormality of pulmonary function tests
5. Any nasal, pharyngeal, or laryngeal finding which precludes bronchoscopy
6. Current use of any medication taken through the nasal or inhaled route including cocaine or other recreational drugs
7. Laboratory evidence at screening of latent M. tuberculosis infection as indicated by a positive ELISPOT response to ESAT6 or CFP10 antigens
8. Clinical, radiological, or laboratory evidence of current active TB disease
9. Previous vaccination with candidate vaccine MVA85A or candidate vaccine FP85A or any other recombinant MVA vaccine
10. Clinically significant history of skin disorder, allergy, immunodeficiency (including HIV), cancer (except BCC or CIS), cardiovascular disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder, neurological illness, psychiatric disorder, drug or alcohol abuse
11. History of serious psychiatric condition
12. Concurrent oral or systemic steroid medication or the concurrent use of other immunosuppressive agents
13. History of anaphylaxis to vaccination or any allergy likely to be exacerbated by any component of the trial vaccine, sedative drugs, or any local or general anaesthetic agents
14. Any abnormality of screening blood or urine tests that is deemed to be clinically significant or that may compromise the safety of the subject in the trial
15. Positive HBsAg, HCV or HIV antibodies
16. Female currently lactating, confirmed pregnancy or intention to become pregnant during trial period
17. Use of an investigational medicinal product or non-registered drug, live vaccine, or medical device other than the trial vaccine for 30 days prior to dosing with the trial vaccine, or planned use during the trial period
18. Administration of immunoglobulins and/or any blood products within the three months preceding the planned trial vaccination date
19. Any other significant disease, disorder or finding, which, in the opinion of the investigator, may either put the subject at risk or may influence the result of the trial or may affect the subject s ability to participate in the trial

## Date of first enrolment
12/11/2013

**Date of final enrolment**
02/02/2015

# Locations

**Countries of recruitment**
United Kingdom

England

**Study participating centre**
**Old Road Campus**
Oxford
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# Sponsor information

**Organisation**
University of Oxford (UK)

**ROR**
https://ror.org/052gg0110

# Funder(s)

**Funder type**
Government

**Funder Name**
National Institute for Health Research (NIHR)

**Alternative Name(s)**
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
United Kingdom

**Funder Name**
Wellcome Trust (UK)

**Alternative Name(s)**

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
International organizations

**Location**
United Kingdom

# 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 | 30/04/2019 | 03/07/2019 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |