



A study evaluating the effectiveness and safety of an investigational TB vaccine in HIV-infected adults

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The vaccine: MVA85A



Modified Vaccinia Ankara

- Poxvirus
- No replication in human tissues
- Good T-cell enhancing vector
- Excellent safety record



M. tb antigen 85A

- Mycolyl transferase
- Major target antigen
- Protective in small animals
- In all environmental mycobacteria
- Doesn't interfere with new diagnostic tests

BCG – MVA85A regimen



Trials in HIV+ participants



	TB010	TB011	TB019
Location	Oxford, UK	Worcester, South Africa	Dakar, Senegal
Dose	10 with 5×10^7 pfu 10 with 1×10^8 pfu	5×10^7 pfu	1×10^8 pfu
Participants:	20 out of 20	27 out of 36	12 out of 24
<i>M. tb</i> coinfectd	4	15	7
CD4 count	>350	>300	>300
Viral load	<100,000	Not specified	<100,000
ARV treatment?	No	24 – No 12 – Yes	12 – No 12 – Yes



Safety of MVA85A in HIV+ participants



- Total of 560 participants vaccinated with MVA85A
 - 59 of whom are HIV infected
- Most participants have mild local reactions
 - redness, swelling, pain, scaling
- Some participants have mild systemic reactions
 - fatigue, headache, feverish, muscle ache
- No difference in local or systemic reactions comparing HIV infected with uninfected participants



Safety contd.



- No clinically significant changes in CD4 count after MVA85A
- No clinically significant changes in HIV viral load after MVA85A
- No signs of immunopathology
- No vaccine-related Serious Adverse Events



Immunogenicity of MVA85A



- Measured using interferon gamma ELISpot and flow cytometry
- Induces high levels of antigen specific polyfunctional CD4+ T cells
- Induces antigen specific CD8+ T cells
- Currently testing samples from HIV trials



Phase IIb efficacy trials



- Infants
 - South Africa
 - 2784 infants
 - All are BCG vaccinated and HIV negative
 - Started vaccinating in July
- HIV positive adults



Phase IIb trial in HIV+ adults



- Proof of concept study in HIV+ adults
 - protection against *M. tb* infection
 - protection against TB disease
 - safety & immunogenicity
- Due to start in 2010
- 24 month follow up
- Sponsored by Aeras
- Funded by EDCTP, MRC and Aeras



Trial design



- 1400 HIV+ adults
 - CD4 >350
 - No history of antiretroviral use
 - Include both *M.tb* positive and negative
- 1×10^8 pfu MVA85A
- Control – candida skin test (Candin)
- Three sites
 - South Africa: Cape Town with Rob Wilkinson
 - Senegal: Dakar with Souleymane Mboup
 - The Gambia: MRC with Martin Ota



Thank you



- University of Oxford team
 - University of Cape Town team
 - MRC The Gambia team
 - Le Dantec team
 - Aeras team
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- Wellcome Trust
 - European Commission
 - MRC
 - Oxford-Emergent TB Consortium
 - EDCTP