Safety and immunogenicity of the candidate tuberculosis vaccine ChAdOx1-85A delivered by aerosol

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An inhaled TB vaccine

- Route of immunisation = route of infection
- BCG does not reliably protect against pulmonary TB
- Mucosal immunisation can generate potent durable immune responses
- Mucosal BCG is protective in mice and NHPs
- Inhalation is a common route of drug delivery
- Needle free
- Not a new idea!

Dijkman et al, NM 2019
ChAdOx1.85A

• Simian adenovirus expressing Antigen 85A
• Well tolerated and immunogenic in a Phase I clinical trial
• Proof-of-concept study to evaluate safety and immunogenicity of ChAdOx1.85A delivered by aerosol.

Wilkie et al, Vaccine 2020
Study Design

**Dose escalation**

- **Group A (n=3)**
  - BCG vaccinated
  - $1 \times 10^9$ ChAdOx1-85A Aerosol

- **Group A (n=3)**
  - BCG vaccinated
  - $5 \times 10^9$ ChAdOx1-85A Aerosol

- **Group A (n=3)**
  - BCG vaccinated
  - $1 \times 10^{10}$ ChAdOx1-85A Aerosol

**Double-Blind Randomisation**

- **Group D (n=10)**
  - BCG vaccinated
  - $1 \times 10^{10}$ ChAdOx1-85A Aerosol
  - Saline IM

- **Group E (n=10)**
  - BCG Naive
  - $1 \times 10^{10}$ ChAdOx1-85A Aerosol
  - Intramuscular (IM) Saline

**Group F (n=10)**

- BCG Naive
- $1 \times 10^{10}$ ChAdOx1-85A Aerosol
- Saline IM

**Study Design**

- **D0, D1, D7, D16, D28, D84, D168**
- Immunogenicity/safety follow-up
- bronchoscopy
Aerosol and IM ChAdOx1-85A is well tolerated

D: Aerosol ChAdOx1-85A, BCG vaccinated
E: IM ChAdOx1-85A, BCG vaccinated
F: Aerosol ChAdOx1-85A, BCG naive
Aerosol CHAdOx1-85A induces peripheral Ag85A, PPD and ChAdOx-1-specific T cell IFN-γ responses

**Ag85A**

- **D**: Aerosol ChAdOx1-85A, BCG vaccinated
- **E**: IM ChAdOx1-85A, BCG vaccinated
- **F**: Aerosol ChAdOx1-85A, BCG naive

**PPD**

Intra-group comparison to D0: ****, p<0.001; ****, p<0.0001. Inter-group comparison with group E: #, p<0.05; ##, p>0.01. PPD responses, groups D/E v F: $$, p<0.01 and $$$, p<0.001

**ChAdOx-1**
Aerosol ChAdOx1-85A induces Ag85A-specific polyfunctional CD4+ and CD8+ T cells in the BAL fluid

D: Aerosol ChAdOx1-85A, BCG vaccinated
E: IM ChAdOx1-85A, BCG vaccinated
F: Aerosol ChAdOx1-85A, BCG naive
Tissue resident lung memory T cells

D: Aerosol ChAdOx1-85A, BCG vaccinated
E: IM ChAdOx1-85A, BCG vaccinated
F: Aerosol ChAdOx1-85A, BCG naive
Kinetics of PBMC ICS Ag85a-specific T cell responses

Ag85a:CD4+IFNg+

% (post-pre)

Study day

D: Aerosol ChAdOx1-85A, BCG vaccinated
E: IM ChAdOx1-85A, BCG vaccinated
F: Aerosol ChAdOx1-85A, BCG naive
Kinetics of serum and BAL Antigen 85A-specific humoral responses

Serum IgG

BAL

D: Aerosol ChAdOx1-85A, BCG vaccinated
E: IM ChAdOx1-85A, BCG vaccinated
F: Aerosol ChAdOx1-85A, BCG naive
Summary

ChAdOx1.85A delivered by aerosol is:
- Well tolerated in BCG vaccinated and BCG naïve subjects
- Induces potent Th1 responses and lung resident T cells in the BAL fluid
- Induces a weak peripheral T cell responses in the blood
- Does not induce significant antibody responses in the BAL fluid or blood

Further studies are needed with this and other candidate TB vaccines delivered by aerosol

These findings are relevant for other respiratory pathogens including SARS CoV2.
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