The C-Tb skin test for LTBI
- Key results from phase III studies

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THE C-Tb CONCEPT

PPD + ESAT-6 CFP-10
C-Tb clinical development

TESAT trials (rdESAT-6)

Toxicology incl. repeated toxicity

SEVEN CLINICAL TRIALS
3,109 participants
→ 723 children
→ 867 HIV-infected

Phase I
Phase I
Phase II
Phase III


Phase III results

Reporting/publications

Embryo-fetal toxicity

Proprietary and Confidential
**C-TB CUT-OFF**

**PPD**
- BCG controls
- TB patients

**C-Tb**
- BCG controls
- TB patients

**ROC curve analysis**

**Optimal cut-off: ≥ 5mm**

BCG controls N=153 (all HIV-)
TB patients N=241 (146 HIV- and 95 HIV+)

Aggerbeck et al, PlosOne 2013; Hoff et al, ERJ 2016
13 sites in Catalonia, Galicia and Basque Country (N=979)

- Unexposed controls (n=263)
- Occasional contacts (circle 2-3, n=299)
- Close contacts (circle 1, n=318)
- TB patients (n=101)
C-Tb IS SPECIFIC IN BCG VACCINATED

C-Tb

Unexposed (n=263)

PPD

BCG vaccinated (N=322)

Occasional contacts (n=299)

BCG unvaccinated (N=505)

Close contacts (n=316)

% of total

Induration (mm)

Test positive (%)

Ruhwald, Lancet RM 2017
### All participants (N=834)

**C-Tb**

<table>
<thead>
<tr>
<th>Test positive (%)</th>
<th>Unexposed</th>
<th>Occasional</th>
<th>Close</th>
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**QFT**

<table>
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<th>Test positive (%)</th>
<th>Unexposed</th>
<th>Occasional</th>
<th>Close</th>
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<thead>
<tr>
<th></th>
<th>C-Tb (+)</th>
<th>QFT (+)</th>
<th>C-Tb (-)</th>
<th>QFT (-)</th>
<th>Total (Σ)</th>
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</thead>
<tbody>
<tr>
<td>+</td>
<td>162</td>
<td>22</td>
<td>184</td>
<td>184</td>
<td>834</td>
</tr>
<tr>
<td>-</td>
<td>27</td>
<td>623</td>
<td>650</td>
<td>650</td>
<td></td>
</tr>
<tr>
<td>Σ</td>
<td>189</td>
<td>645</td>
<td>834</td>
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*P* = 0.5682

Ruhwald, Lancet RM 2017
9 sites in South Africa (N=1190)

- **TB suspects (n=905)**
  - 317 children
  - 588 adults
  - 296 HIV-infected

- **Close contacts (n=185)**
  - 185 children

- **Endemic negative control children (age 5-11y) (n=100)**

<table>
<thead>
<tr>
<th>Location</th>
<th>Investigators</th>
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<tbody>
<tr>
<td>Cape Town</td>
<td>Prof. K. Dheda, Langa Clinic</td>
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<tr>
<td>Cape Town</td>
<td>Prof. A. Diacon and Dr. M. Lourens, TASK</td>
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<tr>
<td>Cape Town</td>
<td>Dr. M. Siebert, Tiervlei Trial Centre</td>
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<tr>
<td>Paarl</td>
<td>Dr. E. Hellstrom, Be Part Yoluntu Centre</td>
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<td>Pretoria</td>
<td>Dr. M. Malahleha, Setshaba Research Centre</td>
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<tr>
<td>Pretoria</td>
<td>Dr. V. Seopela, Synexus Stanza Bopape Clinic</td>
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<tr>
<td>Port Elizabeth</td>
<td>Dr. M. Gani, Primecure Medicentre</td>
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<tr>
<td>Benoni</td>
<td>Dr. I. Mitha, Lakeview Hospital</td>
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</tbody>
</table>

Aggerbaek, Dheda et al, in prep 2017
TRIAL PARTICIPANTS & METHODS

C-Tb and TST randomly applied to each forearm

TB symptomatic (0-65 years) (n=1003, 30% HIV+ve)

Active TB diagnosed (n=75, 45% HIV+ve)
Non-active TB (n=928, 29% HIV+ve)
Asymptomatic pulmonary TB contact < 5 years (n=87)
TEST-POSITIVITY RATE INCREASES WITH AGE

n=699 TB symptomatic participants (excluding HIV-infected)
C-Tb ROBUSTNESS SEEMS SUPERIOR IN HIV INFECTED

- C-Tb has comparable positivity rate in HIV uninfected TB suspects, but significantly higher positivity rate in HIV infected.

- C-Tb performance seems robust in HIV infected with CD4 >100 cells/uL.

Excluding 15% QFT indeterminates
INFLUENCE OF AGE ON INDURATION SIZE

Aggerbaek, Dheda et al, submitted 2017
• C-Tb test results correlate with exposure to *M. tuberculosis*
• C-Tb and QFT have similar positivity rates
• Safety profile of C-Tb is comparable to PPD, local ISRs
• C-Tb is impacted by HIV-infection with low CD4 counts (<100 cells/uL)
• C-Tb induration size is impacted by young age on a level with PPD
• C-Tb deliver IGRA like performance in the field friendly skin test format using a universal 5mm cut off
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• Prof. Åse Bengaard Andersen (DK)

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