A Critical Juncture: progress in TB vaccine clinical development

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New Delhi, India

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Information on candidates in clinical development is self-reported by vaccine sponsors, coordinated by the Working Group on New TB Vaccines and updated September 2017.
Target Populations

• Infants (healthy)
• Adolescents/Adults (healthy)
• TB patients
Increasing focus on adolescent/adult vaccines: to stop the cycle of transmission - will prevent the spread of TB to children as well.

See presentation by R. White (LSHTM)
Therapeutic Indications

• Prevention of TB disease
  – BCG replacement (infants)
  – BCG boost (proximal – infants)
  – BCG boost (distal – adol/adults)

• Prevention of recurrent TB

• TB treatment shortening +/or increased cure rates (adjunct to treatment)
Key Challenges in TB Vaccine Development

- Complicated pathogen and disease
- No known correlate of protection
- Not yet known if animal models are predictive of human TB/protection
- Multiple vaccine candidates in clinical development
- Licensure trials long and expensive
- Severely underfunded
Approaches to Streamlining Efficacy Trials

- Conduct Proof of Concept trials in high-risk populations (see Tait et al)
- Use Phase 2 trials to establish “meaningful biological effect” of vaccine (triaging tool)

Decreasing:
- Risk
- Cost
- Time
Clinical Trial Endpoints

- Prevention of TB disease (POD)
- Prevention of Mtb infection (POI)
- Prevention of TB disease recurrence (POR)
Clinical Trials
(Not an exhaustive list)
## Upcoming Data in TB Vaccine Efficacy Trials

<table>
<thead>
<tr>
<th>PHASE</th>
<th>PARTICIPANTS</th>
<th>EFFICACY</th>
<th>LOCATION</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase III</td>
<td>10000 PPD+</td>
<td>Prevention of disease</td>
<td>China</td>
<td>2018</td>
</tr>
<tr>
<td>Phase II</td>
<td>990 Q-</td>
<td>Prevention of infection</td>
<td>South Africa</td>
<td>1Q2018</td>
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<tr>
<td>Phase IIb</td>
<td>3573 Q+</td>
<td>Prevention of disease</td>
<td>South Africa, Kenya, Zambia</td>
<td>2Q2018</td>
</tr>
<tr>
<td>Phase IIb</td>
<td>650 Q-</td>
<td>Prevention of infection</td>
<td>Tanzania</td>
<td>2018</td>
</tr>
<tr>
<td>Phase II/III</td>
<td>2000 TB+</td>
<td>Prevention of recurrence</td>
<td>India</td>
<td>2020</td>
</tr>
</tbody>
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Anhui Zhifei Longcom: AnHui Zhifei Longcom Biologic Pharmacy Co., Ltd; SSI: Statens Serum Institute; VPM: Vakzine Projekt Management GmbH; SII: Serum Institute of India

Presentation of results this session, M. Hatherill

Modified from M-A Demoitie, GSK
New TB Vaccines are Achievable

Evidence:

- BCG vaccine provides partial protection; for longer duration than previously recognized
- QFT/TST reverters
- QFT/TST resisters
- 90% of infected indivs. remain ‘LTBI’
- LTBI is partially protective against disease

➢ Vaccines can improve on natural immunity (e.g., diptheria, tetanus, pneumococcal conjugate vaccines)
A Critical Juncture

- Improved animal models
- More diverse pipeline under development
- Progress towards a human challenge model
- Novel Phase 2 trial designs in high risk populations
- Imminent results from multiple efficacy trials
- Biomarker/signature/correlate discovery
TB Vaccine R&D is Severely Underfunded

- Annual global cost of TB ~ $20B ($200B over next 10 years)\(^1\)
- Cost to develop one vaccine ~ $1.25B over 10 years\(^2\)
- 2016 funding for TB vaccine R&D: $79M\(^3\)
- 2016 funding for HIV vaccine R&D: $733M\(^3\)

Now more than ever is the time to ensure TB vaccine R&D gets the funding it needs.

Recent Major Funders and Aeras R&D Partners
Current Clinical Sites and Networks

With special thanks to the sites and participants and their families in our clinical trials
Thank You