A randomized, double-blind, dose-escalation clinical trial of MTBVAC compared to BCG Vaccine SSI, in newborns living in a tuberculosis endemic region

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MTBVC is a live attenuated derivative of *M. tuberculosis*
Methods

18 healthy adults

– randomized 1:1 to receive:
  • MTBVAC (5 x 10^5 CFU) or BCG SSI (5 x 10^5 CFU)

– HIV negative, QuantiFERON (QFT) negative, previously BCG- vaccinated

36 healthy newborns

– randomized 3:1 to receive:
  • MTBVAC (2.5 x 10^3 CFU) or BCG SSI (2.5 x 10^5 CFU)
  • MTBVAC (2.5 x 10^4 CFU) or BCG SSI (2.5 x 10^5 CFU)
  • MTBVAC (2.5 x 10^5 CFU) or BCG SSI (2.5 x 10^5 CFU)

– Within 96hrs of birth

– HIV-unexposed, BCG-naïve
Objectives

Primary objective:
To evaluate safety and reactogenicity, and immunogenicity of MTBVAC compared to BCG in infants.

Secondary objective:
To evaluate safety and reactogenicity of MTBVAC compared to BCG in adults.
Infants Schedule of Events

Day 0
- Vaccinate MTBVAC or BCG

Day 7
- AE reporting period
- SAE reporting period

Day 28
- Safety WB-ICS

Day 70
- WB-ICS

Day 180
- QFT WB-ICS

Day 365
- QFT WB-ICS

12HR WB-ICS antigen: MTBVAC

QFT antigens: ESAT-6, CFP-10, TB7.7
117 pregnant women were consented antenatally, and 36 neonates enrolled.

Most frequent reasons for screening failure:
- 9 neonates received BCG at the birthing unit
- 34 neonates were born during DSMB safety review pause
- 10 neonates excluded while awaiting approval of protocol amendment due to BCG SSI unavailability.
MTBVAC is well tolerated

Local Reactions

- **Swelling**
- **Redness**
- **Scarring**

<table>
<thead>
<tr>
<th></th>
<th>MTBVAC $2.5 \times 10^3$</th>
<th>MTBVAC $2.5 \times 10^4$</th>
<th>MTBVAC $2.5 \times 10^5$</th>
<th>BCG $2.5 \times 10^5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swelling</td>
<td></td>
<td></td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Redness</td>
<td></td>
<td></td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Scarring</td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Number of participants recording an episode
MTBVAC is well tolerated

All AE’s - Severity

- BCG $2.5 \times 10^5$
- MTBVAC $2.5 \times 10^5$
- MTBVAC $2.5 \times 10^4$
- MTBVAC $2.5 \times 10^3$

Number of participants recording an episode

- Mild
- Moderate
- Severe
QFT conversion occurred in MTBVAC vaccinated participants

<table>
<thead>
<tr>
<th>Group</th>
<th>M6 QFT +</th>
<th>IPT received</th>
<th>M12 QFT +</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTBVAC 2.5 x 10^3</td>
<td>3 (37.5%)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>n=9</td>
<td>n=8</td>
<td>n=8</td>
<td>n=8</td>
</tr>
<tr>
<td>MTBVAC 2.5 x 10^4</td>
<td>6 (75%)</td>
<td>6</td>
<td>2 (25.0%)</td>
</tr>
<tr>
<td>n=9</td>
<td>n=8</td>
<td>n=8</td>
<td>n=8</td>
</tr>
<tr>
<td>MTBVAC 2.5 x 10^5</td>
<td>7 (77.8%)</td>
<td>6</td>
<td>4 (44.4%)</td>
</tr>
<tr>
<td>n=10</td>
<td>n=8</td>
<td>n=9</td>
<td>n=9</td>
</tr>
<tr>
<td>BCG SSI</td>
<td>0 (0%)</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>n=8</td>
<td>n=7</td>
<td>n=7</td>
<td>n=7</td>
</tr>
</tbody>
</table>

QFT antigens: ESAT-6, CFP-10, TB7.7
Conclusion

MTBVAC is safe in neonates and less reactogenic than BCG, at the same dose level.

MTBVAC $2.5 \times 10^5$ ‘s peak response at D70 was higher than that of BCG SSI.

Further trials in these populations are warranted.