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MTBVAC202: Defining the dose for a multi-centre Phase 3 efficacy trial in infants

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Background: We need safer, more effective tuberculosis vaccines than Bacille Calmette Guérin (BCG). We conducted a Phase IIa dose-defining trial of the live-attenuated Mycobacterium tuberculosis (Mtb) vaccine, MTBVAC, compared to BCG, in South African infants.

Methods: Healthy, HIV-unexposed, BCG-naïve infants were randomised to receive a single intradermal dose of BCG (2·5×10^5CFU, n=24) or MTBVAC (2·5×10^4, 2·5×10^5, or 2·5×10^6CFU, each n=25). Safety endpoints were solicited systemic and injection site, and all unsolicited adverse events (AE), and serious AE (SAE). Immunogenicity was measured using interferon-□□release assay (IGRA) and whole blood intracellular cytokine staining assay. Follow-up was for 12 months.

Results: Ninety-nine infants were enrolled between February 2019 and March 2021. Seventy-eight infants experienced reactogenicity AE (all mild except one grade 2 erythema). Induration, swelling, and erythema were more frequent as MTBVAC dose increased. All reactogenicity events were less frequent in infants receiving MTBVAC 2·5×10^5CFU compared with BCG. Twelve infants (three BCG and nine MTBVAC recipients) experienced 14 vaccine-unrelated SAE, including one death due to bronchopneumonia (MTBVAC recipient). Eight infants were treated for unconfirmed pulmonary TB (four BCG, four MTBVAC 2·5×10^4CFU recipients); one BCG recipient was treated for unconfirmed TB meningitis.

MTBVAC was immunogenic at all 3 doses, inducing predominantly Th1-cytokine-expressing CD4 T cells, which peaked at Day 56. The 2·5×10^5 and 2·5×10^6CFU MTBVAC doses induced similar response magnitudes and were more immunogenic than BCG. Day 56 IGRA conversion was observed in 61 (87.4%) infants receiving any MTBVAC dose, but only 28 (42.4%) remained positive by Day 365.

Conclusion: MTBVAC was safe, well-tolerated, and immunogenic at all 3 doses in South African infants. The 2·5×10^5CFU MTBVAC dose, less reactogenic and more immunogenic than BCG, was selected for the efficacy trial

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Conflicts of Interest

ER, IM, JT, JD, EP are employees of Biofabri , the exclusive licensee of MTBVAC