7TH GLOBAL FORUM ON TB VACCINES | 8-10 October 2024 Rio de Janeiro, Brazil
Driving innovation from discovery to access

MTBVAC dose-finding study, a Phase 1b/2a randomized, controlled, double-blind clinical trial, in young adults in South Africa, with and without sensitization to Mycobacterium tuberculosis

Angelique Luabeya Kany Kany[1], Virginie Rozot[1], Claire Imbratta[1], Frances Ratangee[2], Justin Shenje[1], Michele Tameris[1], Simon C Mendelsohn[1], Michelle Fischer[1], Munyaradzi Musvosvi[1], Humphrey Mulenga[1], Nicole Bilek[1], Ingrid Murillo Jelsbak[3], Esteban Rodríguez[3], Eugenia Puentes[3], Juana Doce[3], Nacho Aguilo[4], Lewis K Schrager[5], Caldwill Pillay[6], Marisa Russell[6], Dereck Tait[6,], Kathryn Rutkowski[5], Devin Hunt[5], Thomas J Scriba[1], Mark Hatherill[1]

[1]*South African Tuberculosis Vaccine Initiative, University of Cape Town, Cape Town, Western Cape, South Africa;* [2]*Department of Biomedical Sciences, Stellenbosch University, Cape Town, Western Cape, South Africa;* [3]*Biofabri, SLU, Porriño (Pontevedra), Pontevedra, Spain;* [4]*Department of Microbiology Pediatrics, Radiology and Public Health, University of Zaragoza, Madrid, Spain;* [5]*IAVI, New York, New York, USA:* [6]*IAVI, Cape Town, Western Cape, South Africa;*

Background: MTBVAC, a live-attenuated Mycobacterium tuberculosis (Mtb) vaccine, was evaluated in South African adults with and without Mtb infection to identify a safe and immunogenic dose level.

Methods: BCG-vaccinated, HIV-negative, South African adults, aged 18-50 years, with/without Mtb sensitization assessed by QuantiFERON-TB Gold-Plus assay (QFT), were enrolled in a Phase 1b/2a randomized controlled clinical trial. MTBVAC vaccine was administered at escalating doses of 5x103, 5x104, 5x105, and 5x106 to 72 QFT-negative and 72 QFT-positive participants, grouped in 8 cohorts. The comparator vaccine was BCG Japan(0,05 mg at 5x105 CFU), administered to 24 QFT-negative and 24 QFT-positive participants. Adverse Events (AE) were evaluated within 7, 28, and 84 days and Serious Adverse Events (SAE) within 365 days. Immunogenicity outcomes included frequencies of Th1 cytokine-expressing MTBVAC-specific CD4 T cells measured by intracellular cytokine staining, and IFN-□ levels measured by QFT.

Results: Between January 15, 2019, and September 07, 2020, 144 out of 485 screened volunteers (38.5% female) were enrolled, 143/144(99.9%) were vaccinated, and 133/143(92.4%) completed the study. Injection site pain, discharge, erythema, and swelling, increased with MTBVAC dose level. QFT-positive MTBVAC recipients reported more injection site reactions [46/48; 95.5% (95%CI 85.7-99.5%)] than QFT-negative MTBVAC recipients [32/48; 66.6% (95% CI 51.6-79.6%)]. No vaccine-related SAE were reported. MTBVAC 5×105 CFU recipients reported a similar rate of related AE (23/24; 95.8%) as BCG recipients (45/47; 95.7%). MTBVAC 5×105 and 5×106 CFU doses induced Th1 cytokine-expressing CD4 T cell responses that exceeded BCG-induced responses in QFT-negative and QFT-positive participants.

Conclusion: Our results suggest that MTBVAC at the 5x105 CFU dose is safe, tolerable, and immunogenic in adults with prior BCG vaccination. These data are pivotal for planned MTBVAC efficacy trials.

Funding Sources
CDMRP, NIH of the US government and IAVI

Conflicts of Interest
None