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Phase 1b/2a clinical trial in adults of novel TB vaccine candidate MTBVAC shows promising results

MTBVAC caused similar or stronger immune responses compared to the Bacille Calmette-Guérin (BCG) vaccine.

NEW YORK, USA, PORRIÑO, SPAIN, CAPE TOWN, SOUTH AFRICA – April 22, 2025 – IAVI, Biofabri, the University of Zaragoza (UNIZAR), and the South African Tuberculosis Vaccine Initiative (SATVI) are pleased to announce today promising results from the IAVI-sponsored A-050 Phase 1b/2a clinical trial testing a novel tuberculosis (TB) vaccine candidate, MTBVAC.

Findings from IAVI A-050, published April 15, 2025 in *Lancet Global Health*, demonstrate that vaccination with MTBVAC caused similar or stronger immune responses compared to the Bacille Calmette-Guérin (BCG) vaccine in adults, and that different doses of MTBVAC were as safe as BCG. The century-old BCG vaccine is the only available TB vaccine and has proven to be ineffective in controlling the spread of TB among adolescents and adults, among whom 90% of TB transmission and disease occurs.

“The world urgently needs a new, effective vaccine that can prevent TB in adolescents and adults if we are to end the devastating TB pandemic, which remains the world’s deadliest infectious disease,” says Mark Feinberg, M.D., Ph.D., president and CEO of IAVI. “The results of this clinical study demonstrate the promise of MTBVAC for this population at a time of renewed attention on the urgent need for new vaccines to curtail the spread of TB. We look forward to our continued collaboration with the study partners in an efficacy trial that began in February 2025.”

The A-050 study investigated the safety profile of MTBVAC at four different doses and how the body’s immune system responds to the different doses, compared to BCG revaccination at a predefined dose. The dose-escalation study took place at SATVI and enrolled 144 healthy HIV-negative

adults, between 18 and 50 years old, with and without previous TB infection who previously received BCG at birth. A previous Phase 1a trial in adults showed that MTBVAC demonstrated a similar safety profile to BCG at a similar dose.

No serious adverse effects were linked to MTBVAC. The expected vaccine side effects with MTBVAC were less than or similar to the expected side effects in the BCG vaccine group, except for the higher doses of MTBVAC. Other side effects were similar for MTBVAC and BCG. Participants who were previously infected with TB showed more expected vaccine side effects than participants who were not previously infected with TB. All doses of MTBVAC caused an immune response, while the highest two doses caused an immune response that was stronger than BCG revaccination. Immune responses were the highest 28 days after receiving MTBVAC or BCG and lasted for at least one year.

“The trial results show that MTBVAC has an acceptable safety profile and generates favorable immune responses,” says Angelique Luabeya, associate professor and principal investigator in A-050, SATVI. “These findings will serve to inform the further development of this candidate in adolescents and adults in countries where TB is endemic. We thank all of the study team members, partnering institutions, and participants who made this trial possible.”

MTBVAC is currently being developed as a potentially more effective and longer-lasting TB vaccine for newborns and for the prevention of TB disease in adults and adolescents. The candidate was designed by the Spanish researcher Carlos Martin, M.D., Ph.D., from UNIZAR and Dr. Brigitte Gicquel, Ph.D., of the Institut Pasteur.

MTBVAC is the only live, attenuated *Mycobacterium tuberculosis* vaccine candidate in the pipeline. Given its derivation from the human, rather than bovine, TB organism, MTBVAC has the potential to maximize the breadth of immune response in vaccinated individuals. If shown to be effective, MTBVAC could have a transformative impact in high TB burden countries, significantly reducing TB-related illness and death, and breaking the cycle of TB transmission. This could deliver far-reaching public health and socioeconomic impacts at the individual, family, community, and societal levels.

“Biofabri and the Zendal Group are proud to collaborate with IAVI, UNIZAR, SATVI, and our other partners to realize the full potential of MTBVAC,” says Esteban Rodríguez, CEO of Biofabri. “Through this partnership we hope to reach our goal of making a TB vaccine available throughout the world.”

If MTBVAC is shown to be safe and effective in late-stage trials, IAVI, in partnership with Biofabri, will ensure that MTBVAC is manufactured and supplied in sufficient quantities to neonates, infants, adolescents, and adults and is accessible at affordable prices in low- and middle-income countries.

The collaborators in the A-050 trial are IAVI; UNIZAR, which developed the vaccine candidate; the Spanish biopharmaceutical company Biofabri, which is the vaccine candidate sponsor; SATVI; and the TuBerculosis Vaccine Initiative (TBVI). Funding was provided by the U.S. Department of Defense through its Congressionally Directed Medical Research Program[i] and the U.S. National Institutes of Health (NIH)[ii].

TB

Since the COVID-19 emergency has ended, TB is again the deadliest infectious disease in the world, killing an estimated 1.25 million people in 2023, about 12% of whom were children. Around 10.8 million people fell ill with tuberculosis in 2023, and the disease is one of the 10 leading causes of death worldwide. A vaccine is needed more urgently than ever.

Drug-resistant/multi-drug resistant TB (DR/MDR TB) is becoming an increasing threat, with about 401,000 cases in 2023. DR/MDR TB treatment is arduous, expensive, and not always successful. A vaccine that prevents TB disease would have a major impact on the DR/MDR TB problem.

MTBVAC

MTBVAC is being developed for two purposes: as a more effective vaccine than BCG for newborns, and for the prevention of TB disease in adults and adolescents, for whom there is currently no effective vaccine.

A Phase 1b trial was conducted in adults and neonates in South Africa to evaluate dose escalation of MTBVAC against a BCG control. The lowest dose (2.5 x 10^3) was discarded due to a lower immune response than the higher doses which were found to be more immunogenic than BCG. MTBVAC had similar safety and reactogenicity to BCG vaccination in infant participants.

Two Phase 2 trials have been completed, one supported by EDCTP and sponsored by Biofabri in infants in South Africa (NCT03536117), and IAVI A-050, detailed in this press release.

A Phase 3 trial (NCT04975178) in infants launched in South Africa, Madagascar, and Senegal in late 2022. A Phase 2 (NCT05947890) safety/immunogenicity study of MTBVAC in people living with HIV (PWHIV) is ongoing. An IAVI-sponsored Phase 2b trial (NCT0627281) in adolescents and adults began in February 2025 at sites in east and southern Africa.

The MTBVAC development partnership:

IAVI is a nonprofit scientific research organization with offices and labs in the U.S., U.K., Europe, Africa, and India that develops vaccines and antibodies for HIV, tuberculosis, emerging infectious diseases, and neglected diseases, with the goal of providing global access. It has contributed to efforts to evaluate most of the leading TB vaccine candidates now in clinical development and has a highly experienced TB vaccine clinical research team in South Africa.

Biofabri is a biopharmaceutical company created in 2008 with the aim of researching, developing, and manufacturing vaccines for humans. Biofabri has a solid technical and scientific capacity in vaccines and immunotherapy. Biofabri belongs to the Zendal group, a Spanish pharmaceutical business group made up of six companies specialised in the development, manufacture, and marketing of vaccines and other biotechnological products for human and animal health.

The **South African Tuberculosis Vaccine Initiative (SATVI**) is a TB research group based at the Faculty of Health Sciences of the University of Cape Town. SATVI is regarded as a worldwide leader in TB vaccine research and has conducted 28 Phase 1–4 trials of 10 different TB vaccine candidates since 2005. SATVI's research focus is understanding the risk for, and protection against, *M. tuberculosis* infection and disease, in order to develop more effective vaccines and preventive strategies for global impact on the TB epidemic.

The **Tuberculosis Vaccine Initiative (TBVI)** is a non-profit foundation that enables the discovery and development of new, safe, and effective tuberculosis vaccines that are accessible and affordable for all people. As the Product Development Association (PDA), TBVI integrates, translates, and prioritizes R&D efforts to discover and develop new TB vaccines and biomarkers for global use. TBVI provides essential services that support the R&D efforts of its partners: 50 partners from academia, research institutes, and private industry in the field of TB vaccines.

The **University of Zaragoza (UNIZAR)** in Spain is the main center for technological innovation in the Ebro Valley. It participates in different exchange programs, collaborating with universities and research centers in Europe, Latin America, and the United States. Microbiologists from the university associated with Centro de Investigación Biomédica en Red Enfermadades Respiratorias (CIBERES) led the research and subsequent discovery of the experimental vaccine MTBVAC. Within the TBVI consortium, the MTBVAC discovery phase has included rigorous clinical characterization by independent laboratories and research groups.

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