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HEALTH SCIENCES

wellcome centre infectious diseases research in africa

FOR IMMEDIATE RELEASE

Candidate vaccine reduces risk of developing active pulmonary TB

Analysis published in the *New England Journal of Medicine* confirms positive results in clinical trial conducted in tuberculosis endemic regions

Today, the *New England Journal of Medicine* published the results of a phase IIb clinical trial testing the candidate tuberculosis (TB) vaccine M72/AS01$_E$[1]. This analysis shows that M72/AS01$_E$ significantly reduced the incidence of pulmonary TB disease in HIV-negative adults who were already infected with latent TB at the time of vaccination. The results demonstrate an overall vaccine efficacy of 50%. The candidate vaccine had an acceptable safety and reactogenicity profile.

The Wellcome Centre for Infectious Diseases Research in Africa (CIDRI-Africa) and the South African Tuberculosis Vaccine Initiative (SATVI), TB research groups based in the Institute of Infectious Disease & Molecular Medicine at the University of Cape Town, are two of 11 sites in Kenya, South Africa and Zambia where the study was conducted. The study was sponsored by the global healthcare company GSK, and conducted in partnership with IAVI, a nonprofit organization dedicated to developing vaccines against HIV and TB.

Tuberculosis is the leading cause of death through infectious disease worldwide and represents a significant public health threat with 1.5 million attributed deaths globally in 2018. In South Africa, the estimated incidence of TB is 520 per 100,000 of the population. The World Health Organization estimates that nearly one-quarter of the global population has latent TB, of whom 10% will develop active pulmonary TB disease. Currently, there is no available TB vaccine with proven, consistent efficacy in adult populations.

Professor Robert J Wilkinson of CIDRI-Africa, Imperial College and the Francis Crick Institute London commented: “We are pleased to have had a part in the conduct and analysis of this study. The results are encouraging. A major task now will be to analyse samples collected from the trial to look for clues how we might do even better. Our previous experience and the combination of Crick and the Wellcome Centre in Cape Town uniquely positions us to play a significant role in this effort, at the same time as contributing to the development of scientific careers in Africa.”

The study assessed the safety and efficacy of M72/AS01$_E$, in adults with latent TB infection, against development of pulmonary TB disease. The trial was conducted in TB-endemic regions in Kenya, South Africa and Zambia and involved 3,573 HIV-negative adults between the ages of 18 and 50 years. Participants who received two doses of either M72/AS01$_E$ or

[1] The GSK proprietary AS01 adjuvant system contains QS-21 Stimulon® adjuvant licensed from Antigenics LLC, a wholly owned subsidiary of Agenus Inc. (NASDAQ: AGEN), MPL and liposomes

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placebo 30 days apart were followed for three years to detect evidence of pulmonary TB disease.

Thirteen of the 1626 participants who received M72/AS01$_E$ developed active lung TB compared with 26 participants of the 1663 in the placebo group, a reduction of 50%.

About the study

This study was a phase IIb, multicentre, randomized (ratio 1:1), double-blind, placebo-controlled study with two groups: M72/AS01$_E$ or placebo. The study was conducted in TB endemic regions, at 11 sites in South Africa, Zambia and Kenya[2] (www.clinicaltrials.gov NCT01755598).

The primary objective of the study was to investigate if two doses of the M72/AS01$_E$ candidate vaccine could prevent adults with latent TB infection from developing pulmonary TB disease, compared with people who received placebo. The study also evaluated the safety, reactogenicity and immunogenicity of the M72/AS01$_E$ candidate vaccine.

The primary results of this study were published in September 2018 in the New England Journal of Medicine (DOI: NEJMdo005415). The primary analysis was performed while the study team remained blinded to individual trial group assignment, whereas the final analysis was performed under fully unblinded conditions. The study's final results confirmed the previously reported clinically acceptable safety profile of M72/AS01$_E$. No patterns were evident in the extended follow-up in terms of occurrence or nature of serious adverse events, fatal events or potential immune-mediated diseases over the study period.

Nearly all participants (99%) in the study consented to enter into a bio-banking study sponsored by IAVI. The samples collected during this study will allow researchers to further investigate the potential vaccine-induced correlates of protection against TB and attempt to identify markers that indicate those at high risk of developing pulmonary TB disease (www.clinicaltrials.gov NCT02097095).

The study was sponsored by GSK and conducted in partnership with IAVI. Funders of IAVI for this study were the Bill & Melinda Gates Foundation, the United Kingdom's Department for International Development, the Directorate General for International Cooperation in the Netherlands, and the Australian Agency for International Development.

About the candidate vaccine

GSK's M72/AS01$_E$ candidate vaccine contains the M72 recombinant fusion protein derived from two *Mycobacterium tuberculosis* antigens (Mtb32A and Mtb39A), combined with the Adjuvant System AS01, which is also a component of GSK's RTS,S/AS01 and Shingrix vaccines.

Results showed M72/AS01$_E$ to have an acceptable safety and reactogenicity profile.

About tuberculosis

[2] Sites in South Africa: SATVI, Task, Setshaba, Aurum-Klerksdorp, Aurum-Tembisa, PHRU, CIDRI-Africa, and Be Part; sites in Zambia: CIDRZ and Zambart; and sites in Kenya: KEMRI.

Nearly one-quarter of the global population is estimated to be infected with the bacterium that causes TB; TB is the leading infectious cause of death worldwide[3]. There were an estimated 10 million new TB cases and 1.5 million deaths attributed to TB in 2018. If untreated, TB often progresses to involve large parts of the lung. An effective vaccine against TB would have a marked impact on TB control, including drug-resistant TB, through interruption of transmission[4,5], and would help achieve the WHO target of ending the TB epidemic by 2035.

About CIDRI-Africa

The Wellcome Centre for Infectious Diseases Research in Africa fosters investigator-led approaches via the overarching scientific objective of combatting infection, especially HIV-1 and tuberculosis, through clinical and laboratory research. Three interlinked platforms support clinical studies in the community, improve the depth of laboratory investigations for infected materials, and advance cutting-edge integration of high-dimensional, big data.

http://www.cidri-africa.uct.ac.za

Contact CIDRI-Africa Director Professor Robert J Wilkinson: robert.wilkinson@uct.ac.za.

About SATVI

The South African Tuberculosis Vaccine Initiative is a research group based at the University of Cape Town and with a field site in the town of Worcester, Western Cape, that focuses on understanding risk for and protection against tuberculosis, in order to develop a new safe and effective TB vaccine.

http://www.satvi.uct.ac.za

Citation

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