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Immunogenicity of an investigational tuberculosis vaccine, M72/AS01E-4, in people living with HIV: a Phase 2, randomized, clinical trial

Lisa Deanne Schlehuber[1], Alemnew F Dagnew[1], Linda L Han[1], Lee Fairlie[2], Craig C Innes[3], Keren Middelkoop[4], Kogieleum Naidoo[5], Michele Tameris[6], Robert J Wilkinson[7], Jintanat Ananworanich[1], Amy Cinar[8], Daniel Bower[9], Justine Sunshine[1], Michael Dunne[1], Alexander C Schmidt[9], Nicole Frahm[1]

[1]Clinical Development, Bill and Melinda Gates Medical Research Institute, Cambridge, Massachusetts, USA; [2]Wits RHI, Univ. of the Witwatersrand, Johannesburg, South Africa; [3]Clinical Research Division, The Aurum Institute, Klerksdorp, South Africa; [4]Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine / Department of Medicine Cape Town, University of Cape Town, South Africa; [5]TB-HIV Treatment Research Programme, CAPRISA, Durban, South Africa; [6]SATVI, University of Cape Town, Cape Town, South Africa; [7]Centre for Infectious Diseases Research in Africa, University of Cape Town, Cape Town , South Africa; [8]Biostatistics and Data Science, Gates Medical Research Institute, Cambridge, Massachusetts, USA; [9]Bill and Melinda Gates Medical Research Institute Cambridge, Massachusetts, USA

Background: The investigational tuberculosis vaccine M72/AS01E-4, provided by GSK, consists of a recombinant fusion protein derived from two Mycobacterium tuberculosis (TB) antigens and AS01E-4 adjuvant. This observer-blind, Phase 2 trial was conducted in South Africa to evaluate safety and immunogenicity of M72/AS01E-4 in 401 participants living with virally-suppressed HIV aged 16-35 years. Participants were randomized 1:1, stratified by site and interferon gamma release assay (IGRA) status, to receive two intramuscular doses of either M72/AS01E-4 or saline placebo, and followed until Day 390.

Methods: The per protocol population (N=273) was evaluated for humoral and cellular immunogenicity. M72-specific IgG serum antibodies were measured by enzyme-linked immunosorbent assay (ELISA) on Days 1 (prior to first dose), 29 (prior to second dose), 57, 210, and 390. The percentage of participants with vaccine-induced M72-specific CD4+ and CD8+ T cell responses and the magnitude of those responses as measured by expression of IFN-γ and/or IL-2 at Days 1, 57, and 390 were assessed. Polyfunctionality including TNF and CD40L expression was also explored.

Findings: Humoral and CD4+ T cell responses peaked after Dose 2 and were sustained at Day 390 in vaccine recipients. Both humoral and cellular immune responses were higher among those who were IGRA-positive (suggesting a boosting effect due to prior exposure) than those who were IGRA-negative (naïve to TB antigens). CD8+ T cell responses remained near baseline indicating a lack of meaningful response.

Interpretation: The 2-dose regimen of the M72/AS01E-4 TB investigational vaccine was immunogenic in people living with well-controlled HIV, showing robust antibody and CD4+ T-cell responses. The results also suggested booster effects of the vaccine in IGRA-positive participants. The outcome of this trial for M72/AS01E-4 led to the inclusion of people living with HIV in an M72/AS01E-4 global registration Phase 3.

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Conflicts of Interest
None