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Accelerating TB vaccine development by "planning for success": The MTBVAC phase 2b clinical trial to prevent TB in African adolescents and adults

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Background: MTBVAC is a live, rationally attenuated vaccine derived from a virulent clinical isolate of Mycobacterium tuberculosis (Mtb). A phase 2b (ph2b) trial of MTBVAC's ability to prevent TB in IGRA+, HIV- persons in South Africa, Kenya and Tanzania is being planned (NCT06272812). This presentation will discuss strategies by which a ph2b trial such as this can be reimagined to "plan for success" and accelerate development, potentially saving resources, time, and lives.

Discussion: MTBVAC represents the only live, attenuated candidate in the TB vaccine pipeline directly derived from a clinical Mtb isolate. MTBVAC is being developed along two clinical pathways: preventing TB disease in infants and in adolescents and adults (A/A). The initial ph1 trials involving adults were conducted in 2013 and 2015 (NCT02013245, NCT02729571). These were followed by a ph1b/2a safety, immunogenicity, and dose-finding trial in 144 IGRA+ and IGRA-, HIV- persons ages 18-60 (NCT02933281). A ph2a trial evaluating the safety and immunogenicity of MTBVAC in A/A living with and without HIV in South Africa is ongoing (NCT05947890). A ph2b trial of MTBVAC to prevent TB in 4,300 IGRA+, HIV- persons in TB endemic regions of sub-Saharan Africa is scheduled to begin in Q3 2024 (the C113 trial; NCT06272812). As designed, the C113 trial will provide data in 2029 to permit a go-no go decision for a phase 3 registration trial. We will describe how relatively small additional investments in a trial such as this can "plan for success", potentially permitting data submission for licensure at the conclusion of this trial in 2029, if supported by sufficiently robust efficacy data.

Conclusion: While an acceleration strategy incurs risk, the approach could reduce the development of a TB vaccine such as MTBVAC by 7 or more years, saving ≥$200 million in development costs and thousands of lives. This approach may serve as a model by which the development of future TB vaccines may be accelerated.

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Conflicts of Interest

None