Project Brief: MESA-TB Gates MRI

Full Title of Study/Programme	A randomized, placebo-controlled, observer-blind, phase 2 study to evaluate safety and immunogenicity of the investigational M72/AS01E *Mycobacterium tuberculosis* (*Mtb*) vaccine in virally suppressed, antiretroviral-treated participants with human immunodeficiency virus (HIV)
Technical Focus Area	Research (16-35 years) HIV positive on HAART with history of INH prophylaxis
Rationale	Published phase 1 and 2 randomized, controlled trials evaluating M72/AS01E vaccination in individuals with HIV who were receiving antiretroviral therapy (ART) show that a 2-dose schedule of the vaccine given one month apart is well-tolerated and immunogenic in this population. This current study intends to confirm that the vaccine is safe, well-tolerated, and immunogenic in a larger population of people with virally suppressed HIV infection in a tuberculosis (TB) endemic region.
Primary Objectives	To assess the safety and reactogenicity of M72/AS01E vaccination
Secondary Objectives	• To assess the safety of M72/AS01E vaccination • To assess the humoral immunogenicity of M72/AS01E vaccination • To assess the cellular immunogenicity of M72/AS01E vaccination
Primary Endpoint/Outcome	• Solicited adverse events (AEs) through 7 days post each dose of study intervention • Unsolicited AEs through 28 days post each dose of study intervention • All serious adverse events (SAEs) through end of study
Secondary Endpoint/Outcome	• Potential immune-mediated diseases (pIMDs) through end of study • Safety laboratory assessments grade 3 or above through end of study • M72-specific antibody concentrations pre- and postvaccination through the end of the study - Frequency, magnitude and polyfunctionality of M72- specific CD*4+ and CD8+ T-cell responses measured by intracellular cytokine staining (ICS) pre- and postvaccination through the end of the study
Study Design (R)	This is randomized, observer-blind, placebo-controlled, clinical trial of M72/AS01E tuberculosis vaccine vs. placebo in approximately 400 males and females between 16 to 35 years of age inclusive, who are living with HIV infection, and are virally suppressed (i.e., viral load < 200 copies per mL) on ART.
Study arms (R)	*Intervention groups*: 2 study groups (M72/AS01E group and placebo group), will each receive 2 vaccinations administered intramuscularly (IM) in the deltoid muscle, preferably of the nondominant arm, one month apart (at Day 1 and Day 29).
Study population (R)	Adolescents 16-35 Years of age

Study sample size (R)	Approximately 400 participants will be enrolled.
Follow up/duration	The study duration for each participant is approximately 390 days, which includes a maximum of 30 days for screening, 2 vaccinations 1 month apart, and 365 days of follow-up post dose 2. Enrolment is expected to take approximately 6 months.
Study/Programme sites	WRHI, CAPRISA, SATVI, Aurum, Desmond Tutu, Ekhaya Vac
Study/Programme duration	Project started Nov -2020 to end ? Dec 2022
Intervention (R)	M72/ASO1E / Normal saline
Operations	
Investigators	Prof Lee Fairlie, Principal Investigator Dr Masebole Masenya, Sub Investigator Dr Faeezah Patel, Sub Investigator Dr Elizea Horne, Sub Investigator
Other Partners & Collaborators	AQVIA, BARC,
Sponsors/Donors	Bill and Melinda Gates Medical Research Institute (Gates MRI)
Linked Sub Studies and post grad projects	
Publications/key presentations to date	
Progress Update as at Jul 2020	Enrolled: 02 On study: 02 Withdrawal 0
Frequency of donor narrative report	
Overall Study/Project Contact	Dr Hermien Gous (hgous@wrhi.ac.za)
Briefing owner and date	Dr Lee Fairlie Mar 2021 reviewed Dr Hermien Gous Mar 2021