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New candidate TB vaccine appears safe and immunogenic in treated TB patients

The results from a clinical trial investigating the use of a candidate vaccine that prevents the recurrence of TB in people who have recovered from the disease, displayed an acceptable safety profile and encouraging evidence of vaccine-induced immune responses when given to cured patients at the end of treatment.

A vaccine which can prevent the recurrence of TB in people who have recovered from TB, could potentially be an important control strategy. Recurrence of TB after treatment is a significant contributor to disease burden in endemic settings, with between 2-9 % of patients developing recurrent TB after completing treatment. Recurrent disease is also a major limiting factor in efforts to shorten and simplify the six-month standard treatment course for drug-sensitive TB and the longer and more toxic treatment regimens for drug-resistant TB. A vaccine that lowers rates of disease recurrence might allow shorter and less toxic TB treatment regimens.

The results from a phase 2 trial of the ID93+GLA-SE candidate vaccine, which has potential for use as a therapeutic vaccine for prevention of post-treatment TB recurrence, have been published by researchers from the University of Cape Town (UCT) and Stellenbosch University, TASK Applied Science, Fred Hutchinson Cancer Research Institute and the Infectious Disease Research Institute.

The paper: Safety and immunogenicity of the adjunct therapeutic vaccine ID93 + GLA-SE in adults who have completed treatment for tuberculosis: a randomised, double-blind, placebo-controlled, phase 2a trial, published in the *Lancet Respiratory Medicine*, reports the results from a trial conducted in the Western Cape of South Africa, which investigated the safety and induced immune responses of the ID93+GLA-SE candidate vaccine between June 2015 and May 2016. Study participants were HIV-uninfected adult TB patients with microbiological confirmation of cure at the end of standard antibiotic treatment.

According to Professor Mark Hatherill, Director at SATVI at UCT, "These results tell us that ID93 + GLA-SE should be tested at the end of treatment as a vaccine to prevent recurrent TB. The next logical step is to test whether the vaccine can be given earlier during TB treatment to improve treatment outcomes".

Professor Rhea Coler, senior investigator at the Seattle Children's Hospital added: "For ID93 + GLA-SE, the groundwork is being laid for follow-on studies to evaluate the vaccine as a therapeutic adjunct to antibiotic treatment in people not only with rifampicin-susceptible TB, but also drug-resistant TB."

Professor Andreas Diacon said that it was an honour for Task Applied Science to be part of this project conducted by leading clinical trial sites in South Africa, where TB is epidemic. "A

vaccine to consolidate cure achieved by daily antibiotics for months would be welcomed by TB patients. Recurrent TB is a major obstacle to shortening and simplifying treatment for TB."

The ID93 + GLA-SE investigational vaccine was developed for prevention of tuberculosis disease in people infected with *M. tuberculosis*; and as an adjunctive therapeutic vaccine to improve treatment outcomes including reduction of post-treatment recurrent TB. ID93 is a polyprotein comprised of four *M. tuberculosis* antigens (Rv1813c, Rv2608, Rv3619c, and Rv3620c) formulated with GLA-SE adjuvant, a synthetic toll-like receptor 4 agonist in a stable oil-in-water emulsion.

Future clinical trials of ID93 + GLA-SE should test the efficacy of post-treatment ID93 + GLA-SE vaccination for the prevention of recurrent drug-sensitive tuberculosis and explore the safety and potential of ID93 + GLA-SE to improve therapeutic outcomes when administered during treatment.

Professor Tom Scriba also from SATVI at UCT noted that TB patients typically already have substantial levels of T cell responses to the TB bacterium, *M. tuberculosis*. It was not known if vaccination after TB cure would be capable of modulating or boosting these pre-existing T cell responses. "The ID93 + GLA-SE vaccine boosted T cell responses to much higher levels than were present before vaccination, while it also induced high levels of antibody responses. These responses persisted at high levels until the end of the trial follow up, which is an encouraging result."

Follow-up trials designed to test the efficacy of the vaccine would be needed to determine if these immune responses are capable of protecting against recurrent TB disease.

The data also support the suitability of ID93 + GLA-SE for further evaluation as vaccine that aims to protect against TB in *M. tuberculosis*-infected populations, a role that will be crucial for interruption of tuberculosis transmission and the success of global tuberculosis control efforts.

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