LETTER TO EDITOR
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Future of TB Prevention: An Alternative To BCG

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Sir,

The global tuberculosis (TB) epidemic is a long-standing public health catastrophe that continues unchecked inspite of, or perhaps because of the certainty that the sole vaccine Bacille Calmette Guerin (BCG) permitted against TB, the world's prime cause of death by an infectious pathogen (World Health Organization,2018c) has been used for nearly an era and has not been improved till date. The poor and variable efficacy of BCG against adult pulmonary TB and latent TB has always been an issue in the elimination together with eradication of the disease.[1]

Newer Tuberculosis vaccines is the need of the hour to achieve the goal of substantially reducing the incidence and eliminate Tuberculosis by 2030 set by Sustainable Developmental Goal of United Nation. WHO has suggested 3 goals in the development of TB vaccines which includes safe, effective & affordable vaccine for adolescent and adult population, improved safety and efficacy in neonates as well as infants and finally to improve TB treatment outcome in all forms.

The mRNA mechanization with lipid nanoparticle distribution systems provides new platforms in the development of tuberculosis vaccine. The novel TB vaccines under trials are categorized as subunit vaccine, recombinant live vaccines, attenuated live vaccine, inactivated and DNA vaccine.[3] Many of the newer vaccine have been in one of the three phases of clinical trials. Currently, the subunit GamTBVac, killed vaccine Mycobacterium indicus pranii, inactivated whole cell Mycobacterium vaccae and the recombinant VPM1002 are the in Phase 3 Clinical trial with promising outcome (Table 1). These are found to be advantageous over BCG by enhance CD8+T-cell production,Superior mixed TH1/TH17 response, accelerated hiring of antigen-specific T cells to the lung contrast to BCG and no negative effect on lowered immune status of the individual (e.g.) SCID.[2,4,7]

The researchers have been still facing challenges in the development of newer vaccines due to lack of proper & reliable animal models, lack of surrogate markers to assess vaccine efficacy, lack of additional funding for clinical trials 4.) Lack of sufficient clinical trial sites 5.) Mycobacterium evokes cellular immune response but majority vaccine against disease evokes humoral immune response.[6]

Table 1: Details of current candidate TB vaccines[1,3]

Vaccine candidate	efficacy/target indication	Study sample
VPM1002	POI, POD, POR	Infants, Children, Adolescents/Adults
Immuvac	POD, Therapeutic	Children, Adolescents/ Adults; Adult TB patients on drug treatment
V7	Therapeutic	Adult TB patients on drug treatment
VaccaeTM#	POD	LTBI (+) Adolescents/ Adults

"*POI – prevention of infection, POD – prevention of disease, POR – prevention of recurrence

Completed Phase 3 trial more than two years ago but results have not been published in peer-reviewed literature as of this writing to the best of our knowledge.

LTBI (+) - Phase 2a trial reportedly in planning, but registry number not found in clinicaltrials.gov or in WHO ICTRP; no TBFLU-04 L primary publications identified in peer-reviewed literature through PubMed search at the time of this writing"[1,3]

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The unprecedented speed in developing, licensing & introducing COVID-19 vaccines provides an important example for an accelerated work-up for the clinical progress and abatement of duration to market for tuberculosis vaccines. Evidence-sharing tools, plan of action created for COVID-19 drug and vaccine research & development should be edged for tuberculosis vaccine research.[7]

To conclude, the future of TB vaccine development looks considerably brighter than before and is now in a pivotal juncture. Limited/lack of pecuniary incentives for development of new vaccines mainly affects the resource curbed underdeveloped nations. Sponsoring to bolster the clinical pipeline & quicken empirical testing of new vaccine candidate is the need of the hour and without an effective vaccine the goal to eliminate Tuberculosis still remains a challenge.

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