GVIRF 2014: Progress towards the development of a TB vaccine	
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Session Outline	**Chair:** Charles Mgone **Opening remarks:** TB is a global infectious disease that has reached epidemic proportions and takes the lives of over a million persons each year. We know we need more than effective drugs and diagnostics to eradicate this disease. **Presentation:** Tom Evans: *Update on Tuberculosis Vaccines – 2014* State of the science of TB vaccine development and summary of key vaccination strategies to control disease. Business case for vaccines being a cost effective, and necessary public health intervention in the fight against TB. **Discussant:** Uli Fruth: *TB Vaccine Development: Challenges & Opportunities* What are the challenges and obstacles that TB vaccine developers and clinical trialists are facing and what pragmatic aspects need to be considered to create medical evidence for the efficacy of vaccines. **Closing Remarks**: Charles Mgone Key messages from the presentations include the need for development of global clinical trials capacity to evaluate vaccine candidates in diverse human populations to gain critical insights into what may constitute correlates of protective immunity.
Objectives of the session	Present progress, challenges and perspectives towards the development of TB vaccines
Main outcome	An update on the status of TB vaccine development, including key strategic shifts in candidate design and selection that will hopefully lead to a successful product, and identification of challenges and knowledge gaps for the development of TB vaccines.
Summary	Tuberculosis (TB) kills 1.3 million people annually, many of whom are women and children. There are 8.5 million new cases of TB each year. Combinations of new and effective products including an effective vaccine will be required to eliminate TB. One hundred million dollars are currently invested in TB vaccine development, compared to $8 billion needed for TB control which highlights that TB prevention could result in dramatic savings in TB care programs globally. Most people who are infected never develop disease, which may indicate that protective immunity against TB is possible. BCG, the only currently available vaccine against TB, does not provide reliable protection against adult pulmonary TB and therefore has not yielded insights into markers of protective immunity in persons who are <u>not</u> naturally able to contain infection. Modelling the potential public health impact of an effective TB vaccine has demonstrated that adolescent and adult vaccination would have the greatest impact to reduce disease. Whether a vaccine can be developed that is better than BCG is unclear. Fortunately, infectious challenge models of in animals have demonstrated superiority of some new vaccine candidates over BCG. Different vaccination strategies are currently being pursued: 1) protection against infection; 2) post-infection protection against disease; and 3) combination of immunotherapeutics or vaccines with chemotherapeutics to shorten the course of therapy or prevent relapse. Several different vaccine candidates are currently being evaluated in clinical trials. In the absence of immune correlates of protection, researchers are exploring the role of immune responses beyond the traditional focus on eliciting Th1-response to include the role of B-cells and probing a variety of protein and non-protein antigens to result in the most diverse vaccination strategies. Furthermore, alternative delivery methods for vaccines, such as pulmonary vaccination, are being explored to identify the role of mucosal immunity for the protection against infection. Aeras now includes testing of advanced vaccine candidates in Non-Human Primate (NHP) models to better assess the effect of vaccination on immune responses and disease outcomes before candidates are advanced into clinical trials. Better animal models and innovative clinical trial designs would help advance the field. Product development could also be improved through expanded research studies of clinical candidates in “experimental medicine trials” that assess endpoints other than those required for licensure of products. These approaches would optimally also include human “challenge” models that are based on BCG as the “infecting” pathogen or employ attenuated strains of *Mycobacterium tuberculosis* (MTB).

	To address the diversity of human TB in endemic countries globally, and account for co-existing morbidities or exposure to environmental mycobacteria that may alter or interfere with vaccine induced immune responses, it is critical to develop trial sites in regions with diverse epidemiological characteristics. To ensure involvement of communities and decision-makers from high-endemicity countries in vaccine trials, work in the TB vaccine development community could be better synergized through a mechanism such as the "Global TBVI" or "CAVD-equivalent," allowing for better global portfolio management and discussions focusing on how to rationally select candidates to progress through the clinical vaccine pipeline.
Key references or quotes	World TB Report, 2013 (www.who.int/tb/publications/global_report/en/) Uli Fruth: TB vaccine development should be bold and aim to do better than nature Uli Fruth: It is critical to develop trial sites in different regions with different epidemiological criteria Uli Fruth: Involve decision-makers from high-endemicity countries. Conduct in places where communities are maximally involved and participate in decision making to ensure that trials are welcome and that data from trials benefit the communities or contribute optimally to research.