Consensus summary report for CEPI/BC March 12–13, 2020 meeting: Assessment of risk of disease enhancement with COVID-19 vaccines

Cornelia L. Dekker
Brighton Collaboration, Task Force for Global Health, Decatur, GA, USA
Email- cdekker@stanford.edu

Abstract

Introduction: A novel coronavirus (CoV), Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in late 2019 in Wuhan, China and has since spread as a global pandemic. Safe and effective vaccines are thus urgently needed to reduce the significant morbidity and mortality of Coronavirus Disease 2019 (COVID-19) disease and ease the major economic impact. There has been an unprecedented rapid response by vaccine developers with now over one hundred vaccine candidates in development and at least six having reached clinical trials. However, a major challenge during rapid development is to avoid safety issues both by thoughtful vaccine design and by thorough evaluation in a timely manner.

Background: A syndrome of "disease enhancement" has been reported in the past for a few viral vaccines where those immunized suffered increased severity or death when they later encountered the virus or were found to have an increased frequency of infection. Animal models allowed scientists to determine the underlying mechanism for the former in the case of Respiratory syncytial virus (RSV) vaccine and have been utilized to design and screen new RSV vaccine candidates. Because some Middle East respiratory syndrome (MERS) and SARS-CoV-1 vaccines have shown evidence of disease enhancement in some animal models, this is a particular concern for SARS-CoV-2 vaccines. To address this challenge, the Coalition for Epidemic Preparedness Innovations (CEPI) and the Brighton Collaboration (BC) Safety Platform for Emergency vACcines (SPEAC) convened a scientific working meeting on March 12 and 13, 2020 of experts in the field of vaccine immunology and coronaviruses to consider what vaccine designs could reduce safety concerns and how animal models and immunological assessments in early clinical trials can help to assess the risk. This report summarizes the evidence presented and provides considerations for safety assessment of COVID-19 vaccine candidates in accelerated vaccine development.

Method:- Since the identification of a novel coronavirus, SARS-CoV-2, as the cause of pneumonia in patients from Wuhan China, a pandemic has erupted, resulting in enormous health care, social and economic disruption to our global society. As of May 17, 2020 there have been 4,708,415 cases and 314,950 deaths worldwide. In rapid response to the pandemic, academic and industry scientists from around the world have initiated efforts to develop vaccines and therapeutics for disease prevention and patient management. The Coalition for Epidemic Preparedness Innovations (CEPI), a global partnership between public, private, philanthropic, and civil organizations, is funding work to develop SARS-CoV-2 vaccines using a variety of technology platforms. Several vaccine candidates are already in Phase 1 studies with others likely to enter the clinic in the next few months.

Results: One of the challenges facing rapid vaccine development for SARS-CoV-2 is the need to adequately assure the safety of these vaccines. One such safety concern is disease enhancement syndrome that occurred in the 1960s with inactivated RSV and measles vaccines. Vaccine-mediated disease enhancement is characterized by a vaccine that results in increased disease severity if the subject is later infected by the natural virus. During early trials with inactivated RSV vaccine, the vaccine did not prevent infection, 80% of those infected required hospitalization and two children died [4]. Lung pathology in patients showed an unexpected inflammatory response with both neutrophils and eosinophils, evidence of immune complex formation and complement activation in small airways [5]. Scientists later learned that the vaccine caused a similar disease enhancement in animals characterized by immunopathology and a T helper cell type 2 (Th2) biased response and antibody responses with poor neutralizing activity [6], [7], [8]. Since that time, the animal models have been relied upon to predict safety for new RSV vaccines that are developed. Of note, the pathogenesis of RSV disease enhancement is distinct from antibody disease enhancement (ADE) which occurs for macrophage tropic viruses, demonstrated most notably for Dengue in humans and the coronavirus feline infectious peritonitis virus in cats, and is directly caused by non-neutralizing or sub-neutralizing antibodies leading to more efficient viral uptake via Fcγ receptor binding

Biography

Cornelia L. Dekker is currently working in a Brighton Collaboration, Task Force for Global Health, Decatur, GA, USA.

This work is partly presented at 40th Global Summit and Expo on Vaccines & Immunology May 18-19, 2020