Session 2: 16:05 – 16:20

Development of Ebanga (mAb114) as a treatment for Ebola virus disease in DR Congo

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Short CV

Dr. Sabue is the SVP of Global Medical Affairs at Ridgeback.
For almost 20 years, Sabue worked in several research projects in the filoviruses area (Ebola and Marburg viruses) including epidemiology, diagnostic, immuno-vaccinology and clinical trials.
Sabue spent a decade of research and training in the intramural program of Vaccine Research Center, NIH.

He is a co-inventor of the EBANGA (aka mab114), a human-derived monoclonal antibody for treatment of Ebola Virus Disease.
Sabue led the first clinical administration of EBANGA to Ebola patients and contributed to the RCT on Ebola therapeutics during the second largest Ebola outbreak in 2018-2020 in DRC.
Sabue contributed to the licensure of EBANGA as one of the only two approved Ebola treatments by the FDA.

Sabue earned his MD and PhD from the University of Kinshasa, and he has a Diploma in Tropical Medicine from the London School of Hygiene and Tropical Medicine. He is Professor of Immunology at the University of Kinshasa.

Abstract

Ebola virus disease (EVD) is a severe disease caused by Ebola virus, a member of the filovirus family, which occurs in humans and other primates. The disease emerged in 1976 in almost simultaneous outbreaks in the Democratic Republic of the Congo (DRC) and Sudan (now South Sudan). There are 6 species of Ebola virus, 4 of which have caused disease in humans: Zaïre ebolavirus (EBOV), Sudan ebolavirus (SUDV), Tai Forest (TAFV) (formerly known as Ebola Ivory Coast), Bundibugyo ebolavirus (BDBV). Since its first appearance, there have been more than 30 EVD outbreaks in sub-Saharan Africa countries and DRC is the most affected countries in terms of the frequency of EVD epidemics. There has been no specific EVD treatment or cure for about 44 years. We aimed at describing the development of a human monoclonal antibody, Ebanga (mab114), as a specific treatment for EVD in DRC. Historical use of polyclonal antibodies to treat filovirus infection has shown some promising success. Convalescent sera were administered to patients with active EVD during the 1995 Kikwit, Zaire outbreak. The mortality reported out of the eight treated patients was 12.5%, a major reduction over the global mortality of EVD cases without specific medical intervention. This observational study served as a proof of concept. Therefore, we sought to isolate mAbs from human EVD survivors, with the goal of identifying antibodies that confer clinical protection. We obtained blood from one survivor of the 1995 EVD outbreak in Kikwit, 11 years after infection. To determine whether the subjects retained circulating antibodies against Ebola virus (EBOV) glyco-protein (GP), we assessed GP-specific antibodies by ELISA and found an EC90 titer higher than control sera by more than a factor of 10. Moreover, the serum displayed potent virus-neutralizing activity indicating that the subject maintained serologic memory against EBOV GP more than a decade after infection. Therefore, we sorted memory B cells from peripheral blood mononuclear cells and immortalized individual clones with Epstein-Barr virus. Forty clone supernatants displayed a range of GP binding; one of them mab114, expressed antibodies with markedly higher neutralizing activity than all others. The sequence from the clone 114 was PCR and antibodies produced by transient transfection. Purified mAb114 was characterized for B cell lineage, binding and structural and molecular properties. When administered as monotherapy to rhesus macaques, mab114 antibody fully protected from clinical symptoms, viremia and death even when given as late as five days after infection. Finally, mb114 has been evaluated for efficacy beside 2 other promising therapies in a RCT study during the largest 2018-2020 EVD outbreak in DRC . Two molecules, including mAb114 , successfully demonstrated efficacy against EBOV by significantly reducing the mortality rate of EVD compared to ZMapp, the control arm. The mab114 (Ebanga) has been approved by the FDA in December 2020 as therapeutic against EBOV.