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Monovalent and multivalent heterologous prime-boost filovirus vaccines: response to the West African Ebola outbreak and preparedness for the future

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Background: The 2014-2016 epidemic of Ebola Zaire (EBOV) in West Africa caused more than 28,000 cases of Ebola Virus Disease (EVD) and more than 11,000 deaths. In response to the epidemic, Janssen accelerated the development of an Ebola vaccine regimen using a heterologous prime-boost combination of two vaccine candidates, Ad26.ZEBOV and MVA-BN-Filo, based on Janssen's AdVac® technology and the MVA-BN® technology from Bavarian Nordic, respectively. Acceleration of vaccine development and production was enabled by effective partnerships – such as the Ebola+ projects supported by the Innovative Medicines Initiative (IMI), as well as the National Institute of Allergy and Infectious Diseases (NIAID), CBMS-Joint Vaccine Acquisition Program (JVAP), and Biomedical Advanced Research and Development Authority (BARDA).

Material/methods: Leveraging the established AdVac and MVA-BN platform technologies, Janssen further developed emergency response capabilities: Ad26.ZEBOV and MVA-BN-Filo were swiftly advanced to clinical trials and manufacturing was rapidly scaled up. Four randomised, placebo-controlled Phase 1 studies have assessed the safety and immunogenicity of Ad26.ZEBOV and MVA-BN-Filo in healthy adults in the EU, US and Africa. Phase 2 and 3 safety and immunogenicity studies in various continents are ongoing. Efficient dialogue with Health Authorities was instrumental in accelerating the programme.

Results: To date, over 2,000 individuals have been vaccinated. Ad26.ZEBOV and MVA-BN-Filo vaccines were well-tolerated and induced robust humoral immune responses in Phase 1 studies when administered as heterologous prime-boost regimens at 28- or 56-day intervals (Milligan ID, et al. JAMA 2016; 315: 1610–23; Anzala O, et al. IMED 2016). Sustained EBOV-specific antibody responses have been detected up to 360 days post-prime. Persisting T-cell responses have also been observed. Leveraging platform technologies expertise and know-how, two million doses of each vaccine were produced through large-scale manufacturing campaigns and stockpiled. Both vaccines are stable for at least 12 months at 2 to 8°C. The vaccines are therefore compatible with typical cold chain requirements and suitable for deployment in remote parts of Africa.

Progress, lessons learned and remaining uncertainties regarding development, regulatory approval, stockpiling and deployment of filovirus vaccines will be presented. The knowledge gained should inform the prevention and control of future filovirus outbreaks.

Conclusions: Based on these characteristics, the Ad26- and MVA-based heterologous prime-boost filovirus vaccine regimens have the potential to play a key role in the prevention and/or containment of future filoviral outbreaks, and in addressing future public health emergency situations. Effective partnerships have expedited vaccine development and facilitated important advances in epidemic preparedness. Furthermore, development of a multivalent filovirus vaccine regimen based on the Ad26 and MVA-BN platforms is underway to address a growing need noted by public health experts since the end of the West African epidemic.