Two-vaccine Ebola regimen shows promise in early-stage clinical trial

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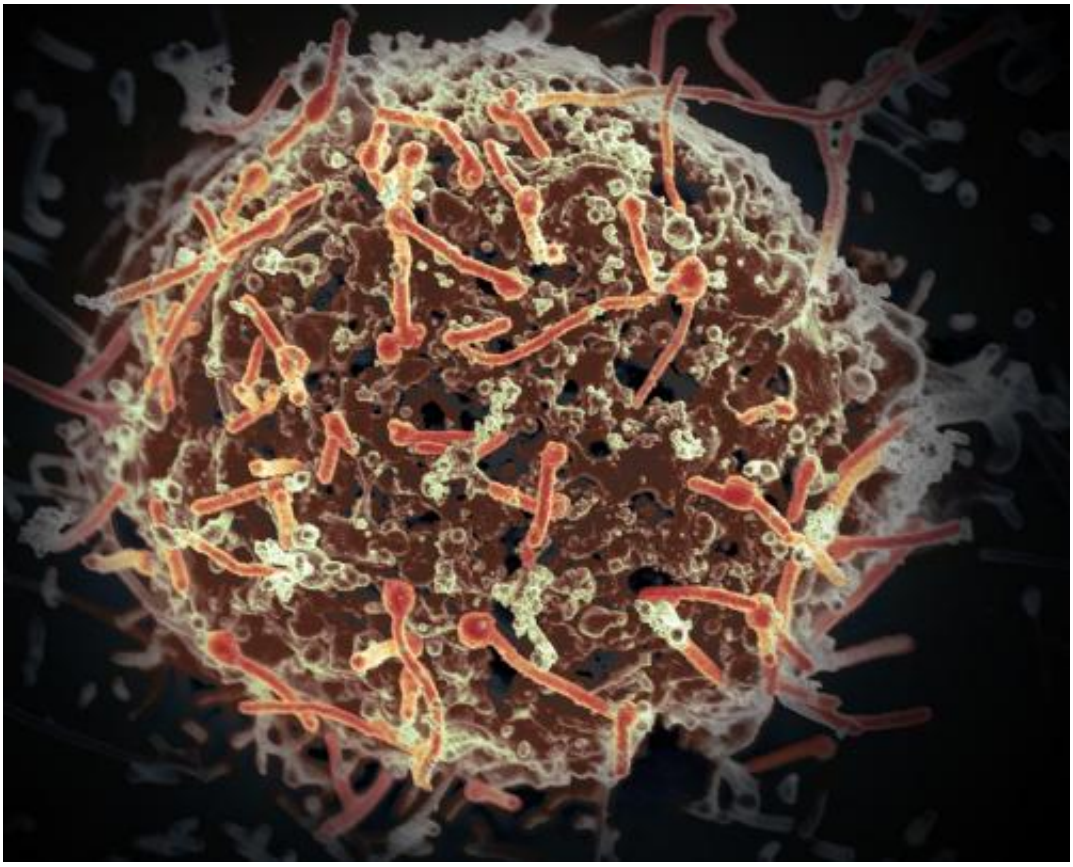

The Ebola virus, isolated in November 2014 from patient blood samples obtained in Mali. The virus was isolated on Vero cells in a BSL-4 suite at Rocky Mountain Laboratories. Credit: NIAID

An immunization regimen using two Ebola vaccine candidates was safe and well-tolerated and induced an immune response in healthy adult

volunteers in a Phase 1 clinical trial. Results from the study are described in the April 19th issue of the *Journal of the American Medical Association*. The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), has supported the development and testing of the two investigational vaccines: Ad26.ZEBOV, developed by Crucell Holland B.V., and MVA-BN-Filo, developed by Bavarian Nordic.

The Ad26.ZEBOV vaccine uses an adenovirus vector, or carrier, to deliver genetic material from Zaire ebolavirus (the virus responsible for the 2014-2015 outbreak in West Africa), prompting the human body to make an immune response. The MVA-BN-Filo vaccine works similarly, using a modified vaccinia virus Ankara vector (MVA) to deliver the same Ebola genetic material, plus inserts for Sudan ebolavirus, Taï Forest ebolavirus and the related Marburg virus. Adenovirus, a common cause of mild respiratory illness in humans, and MVA, a weakened version of vaccinia virus (a poxvirus), have been successfully tested as experimental vaccine platforms.

The trial was conducted in the United Kingdom by University of Oxford scientists from December 2014 to October 2015 and enrolled 87 healthy adults aged 18 to 50 years. The investigators divided 72 participants at random into four groups of 18. On day one, three in each group received a saltwater placebo, and the other 15 received an injection of either Ad26.ZEBOV or MVA-BN-Filo. Participants then received a booster dose with the other vaccine candidate or a second placebo 28 or 56 days later. A fifth group of 15 participants enrolled in a non-randomized group received the Ad26.ZEBOV vaccine on day one. Of this group, 12 participants received the MVA-BN-Filo investigational vaccine 14 days later; three participants did not receive a boost.

The investigators found that both the Ad26.ZEBOV and MVA-BN-Filo investigational vaccines were safe and caused no serious vaccine-related

adverse reactions. All participants who received the Ad26.ZEBOV vaccine first (the prime) followed by the MVA-BN-Filo as a booster vaccination developed and maintained antibodies to Ebola eight months after immunization, and approximately 80 percent of the same group also maintained vaccine-induced T-cells, which help the body fight infection. This sort of durable protection could prove important in areas with intermittent outbreaks of Ebola, in order to provide baseline protection for the community. The vaccine regimens are being tested further in various clinical trials worldwide, including a NIAID-supported Phase 1 trial with Crucell Holland B.V., that is taking place in Rockville, Maryland.

More information: Iain D. Milligan et al. Safety and Immunogenicity of Novel Adenovirus Type 26– and Modified Vaccinia Ankara–Vectored Ebola Vaccines, *JAMA* (2016). DOI: 10.1001/jama.2016.4218

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