CORRESPONDENCE

Cross-Reactive Bundibugyo Antibody Responses after Receipt of Licensed Ebola Vaccines

TO THE EDITOR: The ongoing outbreak of Bundibugyo virus (BDBV) disease in the Democratic Republic of Congo and Uganda has highlighted the lack of licensed vaccines or therapeutics against BDBV. Whether existing Zaire ebolavirus (EBOV) vaccines induce cross-reactive immunity against BDBV remains uncertain. Partial heterologous protection has been observed with rVSVΔG-ZEBOV-GP in nonhuman primates, whereas data for other platforms and in humans remain scarce.[1-4]

We evaluated cross-reactive antibody responses against multiple filoviruses using serum samples obtained from West African adults and children who had been enrolled in the PREVAC randomized clinical trial.[5] We analyzed samples obtained at 28 days and at 3 months after vaccination with rVSVΔG-ZEBOV-GP (Ervebo; single-dose [rVSV] or prime booster [rVSV booster]) or Ad26.ZEBOV/MVA-BN-Filo (Zabdeno and Mvabea [Ad26.MVA]) using a multiplex Luminex assay. Details regarding this analysis are provided in the Methods section in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

We analyzed 179 serum samples obtained from adults and children across vaccine groups at 28 days and 3 months after vaccination. Samples were selected on the basis of availability at the biobank of Institut de Recherche pour le Développement. Overall, the samples reflected the diversity in ages of the patients who were enrolled at multiple centers in the PREVAC trial, which enabled exploratory comparisons across vaccine platforms, age strata, and time points. Among the samples, 55 were collected at 28 days and 124 were collected at 3 months, with no matching of samples between the two time points. (See the Methods section and Table S1 in the Supplementary Appendix.)

Cross-reactive antibody responses against BDBV were detected across all vaccine formulations and at both time points (Fig. 1, Table S2, and Fig. S1). Similar patterns were observed in adults and children. As expected, BDBV responses remained consistently lower than homologous EBOV responses but were detectable after vaccination. In the recipients of the recombinant vesicular stomatitis virus Ebola vaccine (rVSV-EBOV), the response against BDBV (as measured by the median fluorescence intensity [MFI]) was 282 (interquartile range, 164 to 644) at 28 days and 130 (interquartile range, 106 to 436) at 3 months, as compared with 1788 (interquartile range, 832 to 3311) and 1069 (interquartile range, 747 to 1876), respectively, against Kikwit Ebola. Similar findings were observed in the rVSV booster group. After administration of the heterologous Ad26.MVA vaccine, the BDBV response was higher at 3 months (median, 433; interquartile range, 236 to 994) than at 28 days (median, 83; interquartile range, 44 to 131) but remained markedly lower than the corresponding EBOV Kikwit responses.

These findings provide in vitro evidence that these Ebola vaccines induce cross-reactive antibody responses against BDBV. Although the possible protective value of these binding antibodies is unknown, EBOV glycoprotein-binding antibody levels have previously been associated with vaccine-induced protection. Our findings are consistent with those in studies involving nonhuman primates that showed partial heterologous protection after EBOV vaccination. In the absence of a BDBV-specific vaccine, these data support the evaluation of readily available Ebola vaccines during the current outbreak. The single-dose rVSV vaccine, which induced BDBV-binding antibody responses at 28 days and is currently available

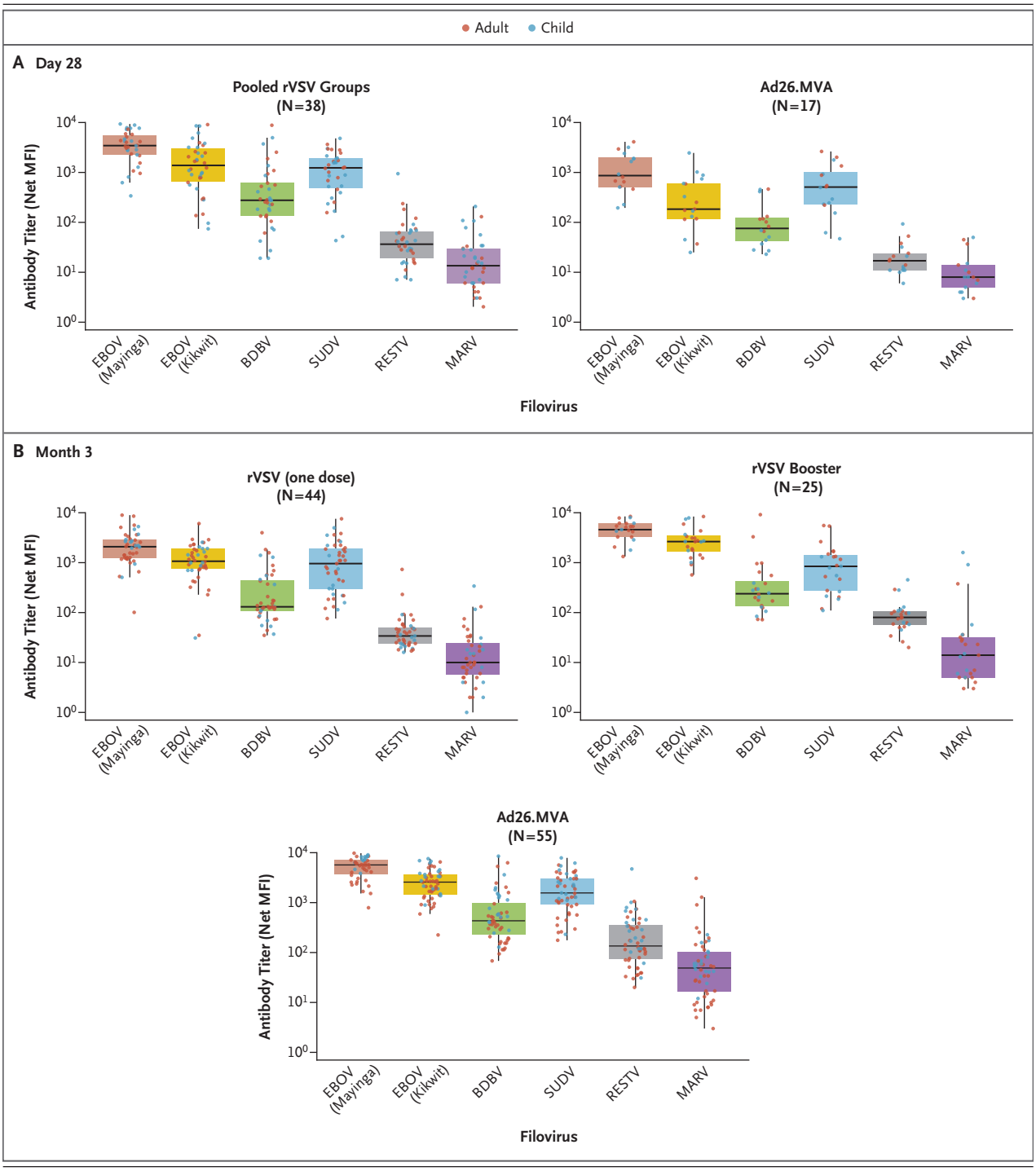

Figure 1 (facing page). Binding Antibody Response at 28 Days and 3 Months after rVSV, rVSV Booster, and Ad26.MVA Vaccination.

Cross-reactive antibody responses against Bundibugyo virus (BDBV) were detected across all vaccine formulations at both 28 days and 3 months, with similar patterns in adults and children. The recombinant vesicular stomatitis virus (rVSV) vaccine and its booster are genetically engineered to replace the VSV glycoprotein with the glycoprotein from a Zaire strain of Ebola virus (EBOV). The Ad26.MVA vaccine uses an adenovirus serotype 26 (Ad26) vector for priming and a modified vaccinia Ankara (MVA) vector for boosting. The response was measured by multiplex Luminex assay as the net median fluorescence intensity (MFI). In each box plot, the horizontal line represents the median, the upper and lower boundaries of the box represent the 75th and 25th percentiles (respectively), and the whiskers extend to the most extreme values within 1.5 times the interquartile range. MARV denotes Marburg virus, RESTV Reston virus, and SUDV Sudan virus.

through the global Ebola vaccine stockpile, represents an immediately deployable candidate that could be evaluated during the ongoing outbreak.

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