Reconsidering the rVSVΔG-ZEBOV-GP vaccine during the 2026 Bundibugyo virus outbreak

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The ongoing 2026 Bundibugyo virus disease (BVD) public health emergency of international concern in DR Congo and Uganda has exposed gaps in preparedness for non-zairense orthoebolaviruses. With BVD vaccines months away, attention has turned to experimental, immunological, epidemiological, and operational evidence supporting the rVSVΔG-ZEBOV-GP vaccine (Ervebo) for potential cross-protection. We believe the available evidence warrants reconsideration of its use in carefully selected high-risk populations while prospectively evaluating its effectiveness against Bundibugyo virus (BDBV).

A recent preprint describing immunogenicity data in 1081 individuals vaccinated with rVSVΔG-ZEBOV-GP in two outbreak-affected regions of DR Congo identified BDBV glycoprotein seroreactivity in approximately half of the participants in Beni, North Kivu, with markedly different response patterns in Mbandaka, suggesting that cross-reactive immune responses might vary across populations.[1] However, these studies measured binding antibody responses only, and immune correlates of protection against BDBV remain undefined.

In non-human primates, a single dose of rVSVΔG-ZEBOV-GP protected three of four cynomolgus macaques against lethal BDBV challenge.[2] A ferret study similarly demonstrated cross-reactive BDBV glycoprotein antibody responses following vaccination with rVSVΔG-ZEBOV-GP,[3] and another recent preclinical study (preprint) reported cross-reactive BDBV antibody responses after vaccination with rVSVΔG-ZEBOV-GP or Ad26.ZEBOV/MVA-BN-Filo.[4] Nevertheless, heterologous protection has not been consistently demonstrated across experimental models, underscoring the need for prospective clinical evaluation.[5]

Preliminary epidemiological observations from the current outbreak merit careful consideration. Based primarily on vaccination histories obtained from routine patient interviews and case investigation forms, nine of more than 1000 confirmed BVD cases reported up to June 24, 2026 in the DR Congo Ministry of Health DHIS2 Tracker database had previous rVSVΔG-ZEBOV-GP vaccination, and all survived. Among the 242 deaths with available vaccination status, none occurred among vaccinated individuals. Additionally, at Mongbwalu General Referral Hospital, a cluster of eight health-care workers developed probable BVD following exposure to a pregnant obstetric patient requiring surgical intervention who was retrospectively suspected to have had BVD in early April, 2026. All three health-care workers with previous rVSVΔG-ZEBOV-GP vaccination survived, whereas all five unvaccinated health-care workers died (Lokudu R, unpublished). Although these observations are limited by incomplete vaccination ascertainment, potential survivor and ascertainment bias, lack of laboratory confirmation, lack of verified vaccination records, and possible unmeasured confounding related to exposure intensity, previous filovirus infection, time since vaccination, and access to care, they represent hypothesis-generating signals warranting prospective investigation.

Outbreak responses frequently require decisions under conditions of incomplete evidence. In a high-mortality epidemic without any current BDBV-specific countermeasures, a "no-regret" public health approach might justify interventions whose potential benefits outweigh foreseeable risks when definitive evidence is unavailable. Public health has adopted similar approaches in the past; for example, malaria vaccines with moderate efficacy have been recommended as part of integrated malaria control strategies because of their projected public health impact when combined with other interventions.[6] Situating rVSVΔG-ZEBOV-GP within this broader framework could also support community engagement, trust, and acceptance.

On May 28, 2026, WHO recommended that rVSVΔG-ZEBOV-GP should not be used outside carefully designed research protocols.[7] Although neutralisation and clinical efficacy data are scarce, this recommendation need not preclude consideration of targeted implementation strategies designed to protect high-risk populations while enabling rigorous prospective evaluation. Importantly, the global emergency stockpile of rVSVΔG-ZEBOV-GP contains approximately 500 000 doses, suggesting that vaccine availability is unlikely to be a major barrier.[8]

Importantly, rVSVΔG-ZEBOV-GP provides proven protection against Ebola virus disease caused by

Orthoebolavirus zairense (EBOV), which circulates in the same ecological setting. During the 2018–20 EBOV outbreak in eastern DR Congo, rVSVΔG-ZEBOV-GP demonstrated 84–98% effectiveness and substantially reduced mortality among vaccinated individuals who developed Ebola virus disease.[9] Risk–benefit assessments should consider not only the uncertain but biologically plausible potential for protection against BDBV, but also the vaccine's efficacy against EBOV and the continued risk of recurrent EBOV outbreaks in the region.

The potential benefits of targeted vaccine deployment—including prevention of severe disease and preservation of essential outbreak response capacity—must be weighed against important risks, including uncertain efficacy against BDBV, diversion of limited resources, and possible erosion of public trust if protection proves limited. However, if the observed signals reflect genuine heterologous protection, carefully designed implementation could reduce morbidity and mortality while generating critical evidence on the extent of that protection.

Implementation should occur within a robust ethical and scientific framework, including independent oversight, transparent informed consent, prospective safety monitoring, and meaningful community engagement through trusted local partners using local languages.[9,10] Communities should understand that no BDBV-specific vaccine is currently available and that rVSVΔG-ZEBOV-GP use is based on possible partial cross-protection from a closely related ebolavirus rather than established clinical efficacy. This intervention should be presented as a complementary, precautionary measure subject to continuous scientific evaluation. Adaptive protocols, prospective observational cohorts, expanded access frameworks, ring vaccination, and embedded immunological studies, could support prospective evaluation within outbreak response.

Health-care workers and front-line responders have the most favourable risk–benefit profile because of their high exposure risk, essential role in outbreak response, and suitability for prospective clinical and immunological follow-up. Household contacts and other high-risk exposures could subsequently be considered through ring-based approaches. Longitudinal immunological studies among vaccinated and unvaccinated exposed individuals could provide important insights into mechanisms and correlates of heterologous protection.

The 2026 BVD outbreak presents a rare opportunity to generate evidence while potentially protecting those at greatest risk. Lessons regarding decision making under uncertainty and integration of research within outbreak response could inform future responses to emerging infectious diseases. If the observed signals of heterologous protection prove genuine, decisions made during this outbreak might be remembered not only for the evidence they generated, but also for the lives they could help save.

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