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Review Article

# Biomarkers of Ebola Vaccine Efficacy and Safety: Comprehensive Review

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**Received:** December 12, 2025; **Published:** January 28, 2026

**DOI:** 10.31080/ECMI.2026.22.01459

## Abstract

Ebola virus is one of the most devastating viruses that belong to the *Filoviridae*. An outbreak of Ebola virus infection is associated with high mortality rates as evidenced during the West Africa outbreak. Although there are no effective antiviral agents against Ebola viral disease, there has been progress in the development of EBOV-associated vaccines. One of the challenges of deploying these vaccines in outbreaks is measuring the correlation of protection as a result of administration of the vaccine. Developing novel biomarkers to measure this correlation would go a long way to develop effective preventive and management strategies. Immune responses in response to EBOV vaccine can be standardised and developed as novel biomarkers. For effective utilization of these biomarkers, developing biomarkers which can be universally utilized should be a priority.

***Keywords:*** *Ebola Virus, Vaccine; Therapeutic; Biomarkers; Clinical Trial*

## Introduction

Ebola virus is a single strand RNA virus that belongs to the genus *Ebolavirus* and family Filoviridae. The genus *Ebolavirus* consist of five species which have been taxonomically designated as follows: *Bundibugyo ebolavirus*, *Reston ebolavirus*, *Sudan ebolavirus*, *Tai Forest ebolavirus,* and *Zaire ebolavirus* [1]. During the 2012-2014 International Committee on Taxonomy of Viruses (ICTV) Filoviridae Study Group, the taxonomy was revised because nearly identical terms can be used to mean different meaning; for example, *Ebolavirus* and Zaire ebolavirus are regarded as taxonomic classifications while Ebola virus is a virus [2].

Of the five species, only Bundibugyo, Sudan, and Ebola viruses have been associated with human diseases. Bundibugyo and Sudan Ebola viruses are associated with outbreaks in mainly South Sudan and Uganda while Ebola virus was initially associated with outbreaks in the Democratic Republic of Congo (DRC), Republic of Congo, and Gabon. The disease caused by any of the specie is referred to as Ebola disease (ED). These viruses have been associated with major outbreaks as a result of human-to-human transmission with about 35, 186 reported cases between 1976 and 2022 (www.cdc.gov/ebola.outbreaks.index.html). Figure 1 outlines the outbreaks associated with Ebola viruses based on historical narrative. The largest outbreak occurred in 2014 during the West epidemic in which 28,610 cases were reported with an estimated 11,325 deaths (39%) [3]. After this largest outbreak, other EVD outbreaks have been reported in Guinea, DRC, and Uganda.

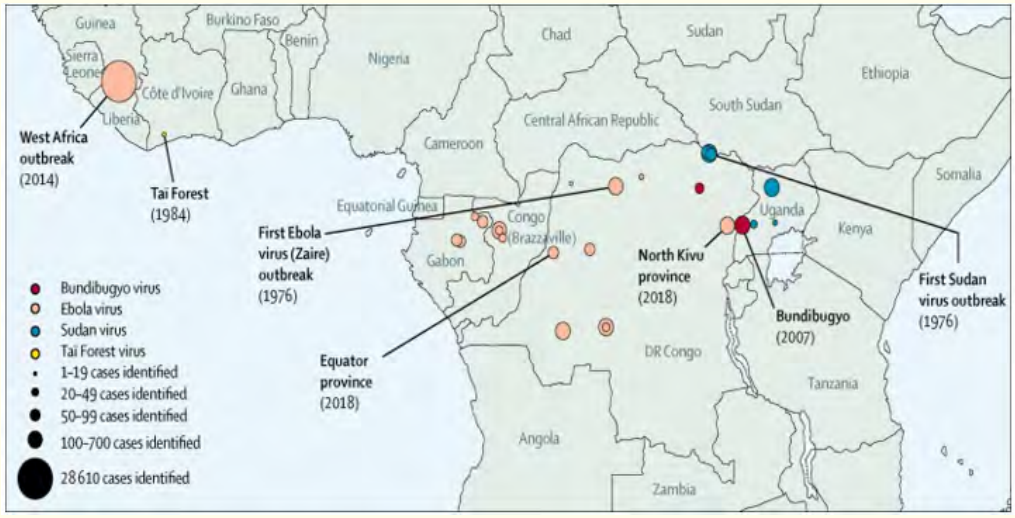


***Figure 1:*** *Outbreaks of Ebola disease (Source: Reference 1).*

Transmission is via person-to-person which occurs through mucous membrane via contact with infected bodily fluid such as vomit, faeces, and blood from infected or symptomatic patient or as a result of coming into contact body of someone who died as a result of EVD. In some cases, droplet transmission has been reported but this is less likely to occur due to the low prevalence of respiratory-associated symptoms [4]. During the West African outbreak, percutaneous transmissions of the virus via sharps objects such as needle-stick, glass-related were reported. Vertical transmission of the virus has also been reported [5].

Clinical manifestations of EVD after an incubation period of 2 - 21 days include high fever, malaise, fatigue, and body aches. Other symptoms are gastrointestinal manifestations such as nausea, vomiting, and diarrhoea. Other less reported symptoms includes cough, dyspnoea, conjunctiva infection, hiccups, or localised pain in the chest, abdomen, muscles or joints [4]. This phase is followed by recovery stage where some patients start to recover. However, others goes into shock due to hypovolemia and systemic inflammatory response which is accompanied by series of hemorrhagic events such as conjunctiva-, petechiae-, gastrointestinal-mucosal-bleedings and continuous discharge after venepuncture [1]. However, it must be stated that during the West Africa outbreak, haemorrhagic manifestation was not common. Neurological manifestation has been reported although they are rare. These include confusion, delirium, and convulsions. Some cases of EBD-associated encephalitis have been reported [6]. Dysphagia, throat pain, and oral ulcers are some late clinical manifestations. The prognosis is if a patient survives this shock phase, there is gradual recovery. However in rare cases, patients who are recovering experiences sudden death due to cardiac arrhythmias [1]. Among pregnant women, there have been reported cases of spontaneous abortion which is followed by bleeding and preterm labour. Stillbirth is associated with late acquisition of the virus in pregnancy [1].

Diagnosing EVD is based on patient showing symptoms that meet the criteria of EVD case definition as outlined by the World Health Organization (WHO) [7,8]. Real-time reverse transcription polymerase chain reaction (RT-PCR) can be used in diagnosing viral RNA from clinical samples [9]. The sensitivity of the molecular evaluations is dependent on the viral load; specimen obtained within 3 days of onset of symptoms may lead to false negative results as a result of undetected viremia during the early clinical phase. In such circumstance, another blood sample should be obtained for RT-PCR 3 days after the onset of symptoms [10]. Point-of-care (POC) rapid diagnostic tests (RDTs) have been suggested but lack of sensitivity is a burden. In summary, when the virus is detected by specific antigen diagnostic tests or by IgM antibodies, it should be confirmed by RT-PCR [4].

Current management strategies consist of supportive care and where possible providing critical care. Therapeutically, investigational therapies were used during the West Africa and subsequent outbreaks. The aim of such interventions was to reduce the replication of the virus to hinder inflammatory storm that is triggered by the viral expansion which allow the innate and adaptive system to mount effective immunological response to enable clearance of the virus.

## Current vaccine against EVD

During the 2014 West Africa outbreak, novel vaccine platforms were developed resulting in rapid acceleration of provision of license. As suggested ideal EVD vaccine should be able to provide rapid protection after a single-dose immunization, efficacious when administered after exposure, and be multivariant by providing protection against all strains and species of Ebola viruses. Some of the vaccine platforms used was able to provide prophylactic protection in non-human subjects [11] such as alphavirus replicons, human adenoviruses, etc (Figure 2) [17]. Table 1 outlines some current EBOV vaccine in clinical trials as of 29 November 2025; these includes virus-like particles, replication incompetent adenovirus serotype 5 vectors, Venezuelan equine encephalitis virus replicons, recombinant vesicular stomatitis virus (rVSV), and replication-competent recombinant human parainfluenza virus 3 (rHPIV3) [12]. Of the described vaccine platforms, three were the most promising: rVSV-ZEBOV/Ervebo, Zabdeno/Mvabea (Ad26-ZEBOV/MVA-BN-Filo) and cAd3-EBOZ. All the three vaccine platforms expressed the virus glycoprotein (GP) antigen to induce immune response. The GP protein is the main surface protein of EBOV that is associated with attachment, fusion, and entry into target cells which make it an attractive therapeutic target because it is recognized easily by the immune system making a target for neutralizing antibody response [18]. Because these vaccine platforms uses vectors, some disadvantages have been reported, including problem of manufacturing, requiring cold chain, and difficulty in adapting to new viral variants [18]. Figure 3 presents the leading EBOV vaccine platforms.

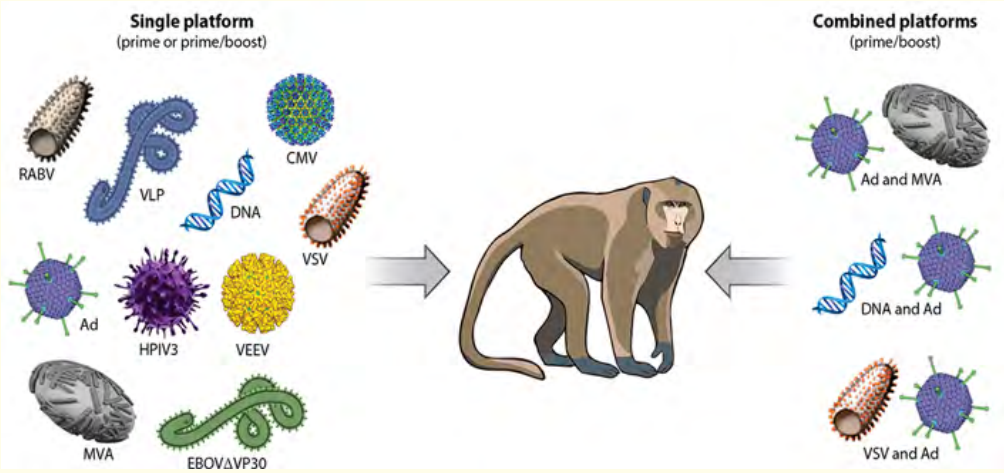


***Figure 2:*** *Various vaccine approach in nonhuman primate models with either complete or partial efficacies. Abbreviations: Ad: Adenovirus; CMV: Cytomegalovirus; EBOVΔVP20: Ebola Virus Lacking the VP30 Gene; HPIV30: Human Parainfluenza Virus Type 3; MVA: Modified Vaccinia Virus Ankara; RABV: Rabies Virus; VEEV: Venezuelan Equine Encephalitis Virus; VLP: Virus Like Particles; VSV: Vesicular Stomatitis Virus (Source: Bio Render).*

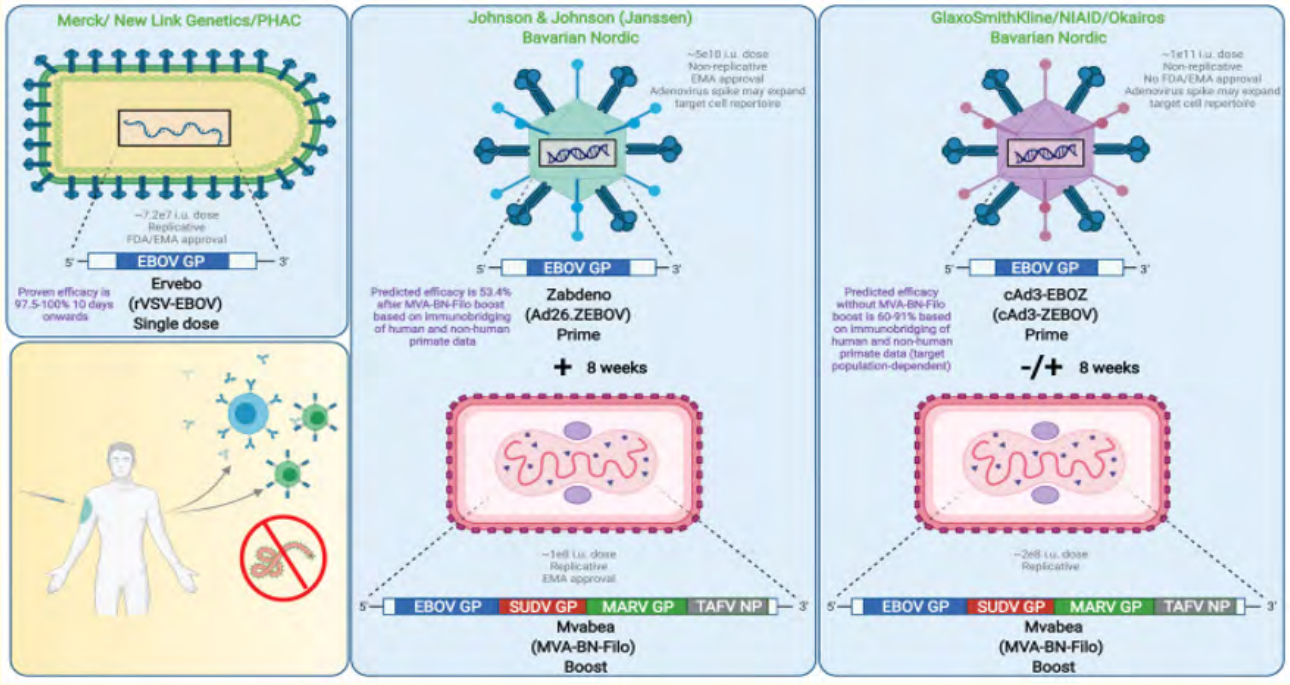


***Figure 3:*** *Advanced EBOV vaccine platform (Source: Biorender).*

Several studies have been undertaken to evaluate the efficacy of these vaccine platforms. Clark., *et al*. in a randomized, doubled-blind, placebo-controlled, phase 1 clinical study used the vaccine candidate consisting of rVSV vector which expressed Ebola virus glycoprotein (EBOV-GP) [13] instead of VSV G protein. Three cohorts were enrolled to evaluate the vaccine based on low-, intermediate-, and high-doses. They concluded that the vaccine was well tolerated at all doses that were evaluated and it was immunogenic despite high degree of attenuation. They therefore suggested that based on the safety and immunogenicity of this vaccine platform, phase 1-2 clinical studies at dose $2x10^6$ and higher single dose and tow-dose regimens should be considered. A previous study reported that this vaccine was effective in inhibiting the transmission of EBOV in a phase 3 clinical studies [14,15] with an acceptable adverse event profile [16]. The European Medicines Agency recommended it conditional approval in November 2019 under the name Ervebo.

The Zabdeno/Mvabea vaccine on the other hand utilized both AdVac and MVA-BN technologies which is administered in two doses: Zabdeno consisting of Ad.26. ZEBOV which is administered first followed by Mvabea consisting of MVA-BN-Filo which is administered approximately 2 weeks later [19]. This means it is not suitable for outbreak response where immediate protection is essential since it has to be administered in two doses. The Zabdeno consist of adenovirus serotype 26 (Ad.26) that expresses EBOV GP instead of replication-essential adenovirus early 1 region. Unlike Ervebo vaccine, the Zabdeno vaccine is unable to replicate in humans. This characteristic makes it an attractive platform for preventive strategy. However, higher doses are required to induce protective immune response. Adenovirus is a ubiquitous virus which is associated with human disease. It is therefore possible that many individuals possess pre-existing immunity against the virus vector, especially in EBOV-endemic areas may be impacted by this vaccine [20]. However, Milligen., *et al.* reported that immune responses of Zabdeno/Mvabea-vaccinated individuals were not distinctly different between seronegative subjects and those showing baseline Ad26 seropositivity [21]. Mvabea is made of modified Vaccinia Ankara (MVA) that encodes GPs from EBOV, SUDV, Marburg virus, and TAFV nucleoprotein. Because it consists of multiple Filovirus vaccine, it can be used in targeting multiple EBOV species. It can serve as an ideal model for effective preventive strategy.

Although no studies has evaluated the protective ability of Zabdeno/Mvabea against MARV and other EBOV species, preclinical studies has shown that prime-boost immunization using Zabdeno/Mvabea is associated with full protection among trial nonhuman primates against challenge of EBOV. Because data on the efficacy is not available, Zabdeno/Mvabea was approved based on clinical immunogenicity report that showed efficacy and immunogenicity in nonhuman primates. A Zabdeno/Mvabea booster is recommended for subject at high risk of EBOV exposure after the completion of their 2-dose vaccine regimen after mother than four months [18].

cAd3-EBOZ was developed with or without MVA-BN-Filo by the NIAID/NIH in partnership with Okairos [19]. This vaccine platform is similar to Zabdeno/Mvabea but the first dose is made of attenuated chimpanzee adenovirus (cAd3). Phase I/II clinical studies has shown that the vaccine is well tolerated and immunogenic. A study by Ewer., *et al*. reported that when cAd3vaccine was boosted with MVA, it induced B- and T-cells immune responses to ZEBOV. It was superior to those induced by cAd3 vaccine alone. This finding was consistent to a study by Tapia., *et al*. who reported that boosting cAd3 with MVA-BN-Filo. However, it was found to be a complicated regimen, leading to long-lived protection. Dolzhikov., *et al*. also reported of similar effect after boosting. This suggests boosting could improve protection and duration of immunity [22-24].

| Start date | Status | Phase | Location | Study ID | Reference |
|---|---|---|---|---|---|
| 2015-12-22 | Completed | Phase 1 | United Stated | NCT02718469 | 13 |
| 2017-05-17 | Completed | Observational | United Kingdom | NCT03140774 | 21 |
| 2019-12-18 | Completed | Phase 2 | DRC | NCT04186000 | 25,26 |
| 2015-10 | Completed | Phase 2 | Sierra Leone | NCT02575456 | No results |
| 2015-06-15 | Completed | Phase 2 | France | NCT02416453 | 27 |
| 2010-02 | Completed | Phase 1 | Uganda | NCT00997607 | 28 |
| 2015-09-21 | Completed | Phase 1 | United Kingdom | NCT02495246 | No results |
| 2017-08-03 | Complete | Phase 4 | Guinea | NCT03072030 | No results |
| 2014-12 | Completed | Phase 1 | China | NCT02326194 | 29,30 |
| 2015-09-30 | Completed | Phase 3 | Sierra Leone | NCT02509494 | 31,32,33 |
| 2014-10 | Completed | Phase 1<br>Phase 2 | Switzerland | NCT02289027 | 62 |
| 2014-09-17 | Completed | Phase 1 | United Kingdom | NCT02240875 | 63,64 |
| 2017-05-17 | Completed | Observational | United Kingdom | NCT03140774 | 65,66 |

***Table 1:*** *Overview of some completed clinical trials of EBOV Vaccine candidates (29/11/2025) (www.clinicaltirals.gov).*

## General view of biomarkers

Biomarkers can be use to predict the efficacy and immunogenicity of a vaccine. Biomarkers can therefore be defined as "a marker that is objectively measured and evaluated to predict the normal biological processes, pathogenic processes, or pharmacological response to a therapeutic intervention" [34]. Biomarkers are therefore used in screening, diagnosing, staging, monitoring of diseases and therapeutic interventions. Certain techniques have been reported to be used for identification of biomarkers. The first process is to understand the pathophysiology of a disease and the factors that establishes it. For example, when studying the biomarkers of heart failure, it has been found that biomarkers were associated with mechanisms that play role in the aetiology of heart failure. Early markers can be used to predict and diagnose diseases, select therapeutic regimens or evaluate the progression of disease [35].

## Novel biomarkers for EBOV vaccine efficacy

Identification of antibody-based biomarkers has been described in literature. Antibody-based have been used in elucidating the efficacy of hepatitis B virus (HBV) vaccine where it was found that a monoantibody, 5F11 was a biomarker of efficacy of HBV vaccine [36] and HIV vaccine [37] where the magnitude and breadth of neutralizing multiple strains of HIV were identified as key biomarkers for HIV vaccine efficacy. Although several EBOV vaccine candidates are available (Figure 3), undertaking randomised clinical trials to evaluate the efficacy of vaccine candidates in clinical randomised trials is a major challenge especially during an outbreak. However, few studies have elucidated the efficacy of EBOV vaccine candidates. A study by Poetsch., *et al*. investigated pre-existing and vaccine-induced vector immunity consisting of thirty subjects involved in Phase-1 VSV-EBOV vaccine study. Humoral and T-cell mediates immune responses were identified which can serve as biomarkers of EBOV vaccine efficacy [38]. A study by Lambe., *et al*. aimed at detecting vaccine-induced antibodies to EBOV MVA-boosted vaccine in oral fluid reported that detection of IgM can be used as a marker for early detection of immunological response to an EBOV vaccine in serum and oral fluid while IgG can be used as differential marker for recent infections vs. vaccine response during field evaluation or studies [63]. Furthermore, Ewer., *et al*. also reported by boosting a monovalent chimpanzee adenovirus Ebola vaccine with MVA, resulted in increased glycoprotein-specific CD8+ T cells while there was significant increase in neutralizing antibodies among participants who receiving boosting regimen [64]. This means glycoprotein-specific CD8+ T cells can be used as marker to EBOV vaccine that has been boosted with MVA while the presence of neutralizing antibodies can serve as marker to assess the efficacy of the vaccine after boosting. Winslow., *et al*. also evaluated immune responses associated with novel adenovirus type 26 and modified vaccinia virus Ankara-vectored EBOV vaccines at one year. They found that at days 360, IgG associated with EBOV was induced while vaccine-elicited T-cell responses were persistent in 60% and 83% of the study participants who were initially given Ad26. ZEBOV followed by a booster dose of MVA-BN in comparison to approximately 69% to 100% of those getting reverse regimen. These data can be used to assess the efficacy of these vaccines one year after been administered. However, the study of Winslow., *et al*. had a prominent limitation; the study participants were Europeans. More studies are needed to evaluate the efficacy among individuals from sub-Saharan Africa and other risk areas since immune response may differ from Europeans. Rechtien., *et al*. used system vaccinology to evaluate early innate immune response that was induced by rVSV-ZEBOV vaccine. They identified early innate biomarkers that correlated with antibody response when rVSV-ZEBOV vaccine was administered and rapid and robust increase in cytokines levels was observed. These included IP-10, MCP-1, and MIP-1β; with maximum plasma level peaking on first day after vaccination (Figure 4) [67]. These markers; especially IP-10 can be used in future field studies when the efficacy of EBOV vaccine needs to be evaluated after day 1. Similarly, administrating of rVSV-ZEBOV vaccine was linked with significant and early induction of NK cells, monocytes, and DCs at day 1 and day 3 post-vaccination [67]. Just as in the induction of cytokines, these markers can be used in field studies for early assessment of EBOV vaccines.

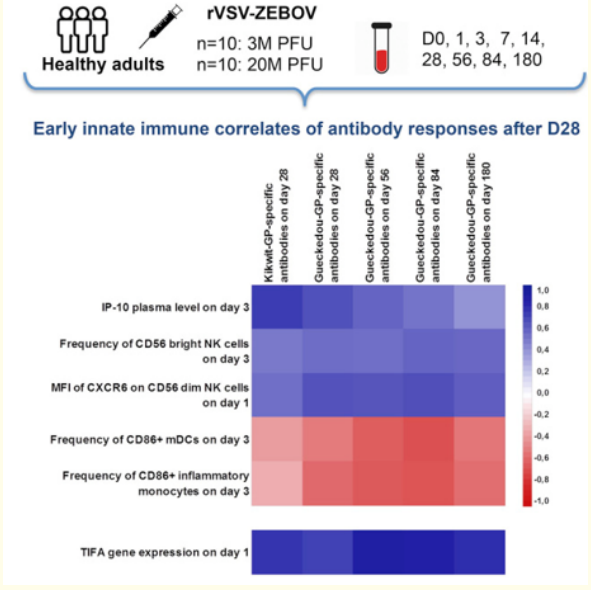


***Figure 4:*** *Early immune correlation after administering rVSV-ZEBOV vaccine (Source: 67).*

## Samples used for identification of vaccine response biomarkers

The type of samples used for identifying biomarkers in response to vaccination is essential. Blood is the main source of biomarkers which is accessible among human beings. This allows the study of circulating cells, serum (antibodies), and plasma (soluble factors) [39]. The peripheral blood mononuclear cells (PBMCs) is also an essential medium for the identification of vaccine response biomarkers as it can be used in measuring immune activity in other tissues as outlined in a study by DeGottardi., *et al*. in which circulatory $CXCR5^{+}$ $CD4^{+}$ T cells in the peripheral blood was used to predict biomarker after yellow fever vaccination [40]. Other researchers have also utilized blood samples in identifying association of protection for series of vaccines such as post antibody IgG levels in *Bordetella pertussis* vaccination, humoral response in smallpox vaccination, and cell-mediated immunity for Zoster vaccine [41-43]. Sera was also utilized in several studies such as Julkunen., *et al*. who utilized paired sera from twenty patients who evaluated antibody response to mumps vaccine from sixteen individuals who were vaccinated with live attenuated mumps virus vaccine as well as twelve individuals who were vaccinated with formalin-inactivated virus vaccine [44]. Unlike peripheral blood, other human tissues can be used as sample to predict biomarkers of vaccine response. However, these tissues are not easy to access without invasive techniques. It has limitation in that it cannot be deployed in large-scale studies. Furthermore, preclinical model can be used as it allow access to all organs which can result in the identification of relevant biomarkers; such as use of liver for the identification of biomarkers as reported by Monath for yellow fever 17D vaccine [45]. Mucosal immunity is also used in measuring protection conferred by some vaccines. This means samples such as bronchoalveolar lavages and lung lymph nodes can be used in identification of biomarkers of vaccine response [46]. Cervicovaginal secretion is another predictive sample for identification of novel biomarkers. Pattyn., *et al*. in a review study reported that human Papillomavirus-specific antibodies were measured in cervicovaginal secretion based on HPV vaccine response [47]. Finally, with EBOV infection, bodily fluids are the optimum sample for identifying biomarkers of vaccine response; in addition to macrophages and monocytes [48].

To conclude, different type of biological samples indicates different facet of immune response. This means it can influence biomarkers which can then be identified. Studies are needed to identify different sample models for typing vaccine response in EBOV vaccine programs.

## Epigenomics for assessing EBOV vaccine response

A vaccine usually induces adaptive a response via the adaptive immune system which is represented by humoral and cell-mediated immunity. To establish the role of vaccine-elicited immune response on protection to EBOV infection and disease is essential in vaccine studies. The correlation of protection measures the threshold at which immune response beyond where EBOV infection and disease does not happen. However, in situation where the immune response takes place among the vaccinated group, validation of correlation of protection or immune response as a true marker with causative role is usually a problem [49]. To enable a vaccine developer to gain approval by a regulatory body, the developer must provide evidence of the vaccine been highly purifies and exhibits the induction of immune response. Several techniques have being used in evaluating the humoral and cellular immunity in vaccine studies. These include ELISA, Cytotoxic T-lymphocyte (CTL) assay, flow cytometry, ELISpot assay, etc [50]. All the assessments techniques have some advantages and disadvantages (Table 2).

While these approaches are good for elucidating vaccine responses, novel technique are required that would be essential in understanding and improving vaccine response. This can be achieved by using epigenomics which studies epigenetic modification. Growing data shows that both vaccination and natural infection have a role in changing the epigenome thereby regulating both the initial immune response and increase disease risk. Studies have shown that certain pathogens such as human Papilloma virus, hepatitis C virus, and *H pylori* are associated with the development of cancer through induction of epigenetic modifications and it has been suggested that

| Method | Advantages | Disadvantages |
|---|---|---|
| ELISpot | Quantitative<br>Can be standardized<br>Cost effective<br>Adaptive to different cell types and cytokines | Just one cytokine per sample<br>Doesn't give information about specific cell type<br>Normally require cell expansion<br>Complex procedure |
| ELISA | High sensitivity and specificity<br>Ease to use<br>Able to analyze complex samples | Potential for false/negative results<br>Need specialized equipment<br>Antibody instability |
| Flow cytometry | Rapid analysis of numerous cells at the same time<br>Detailed characterization and separation of cell populations | High cost<br>Specialized equipment required<br>Need for single-cell suspensions |
| CTL assay | Ability to assess CTL function directly<br>Provide information about specific antigen recognition<br>Useful in identifying potential immunosuppressive agents such as vaccines | Challenges in accurate evaluation of target cells<br>Potential operator error<br>Limitation in detecting full complexity of CTL-mediated cytotoxicity |

***Table 2:*** *Advantages and disadvantages of some techniques used to study vaccine response.*

one of the scopes where epigenetic can play a role is the effect of heterologous effect of vaccines [51]. Although there is no study that evaluates association of epigenomics to EBOV vaccine response, several authors have evaluated vaccine response using epigenomics. In a review study, Bannister., *et al*. proposed that heterologous effect of BCG vaccine might be due to epigenetic reprogramming of the innate immune cells and the development of innate immune memory. BCG is known to be effective among neonate as it is associated with significant survival in high mortality environment and beyond for the protection against tuberculosis. Among the elderly, it was found that poor humoral immune response to influenza vaccine uptake was associated to immunosenescence (age-associated decline in the function of the immune system) [52]. By understanding the mechanism of immunosenescence in vaccinology, it would not only help us measure the immune responses of a vaccine but also able to improve the efficacy of vaccine to enable us counter the impact of immunosenescence. Gensous., *et al*. also suggested that epigenetic landscape can be of benefit in understanding the biological basis of vaccine response during aging and this might be prospective biomarkers of this process. This conclusion was based on study that compared influenza vaccine response among the older and younger population which the data showing epigenetic remodelling among the vaccine responders who were over fifty years old [53]. In view of this, an essential area of research is to understand the effect of immunosenescence in EBOV vaccination and whether immunosenescence have a role in determining the period of vaccination after previous vaccine administration.

## Models for predicting EBOV vaccine response

Predicting immunological response to vaccine is essential for improving development of vaccine and optimizing existing vaccines. Identification of biomarkers that measures correlation response to vaccine is an important objective [54]. Elucidation of vaccine response and its mechanism of action or evaluation of optimal dosages have been undertaken for several infectious diseases such as influenza fever, Zika, and recently COVID-19 [55]. With current EBOV vaccine platforms, binding concentration of antibodies is regarded as hallmark of good correlation of protection [56]. Elucidating the vaccine response by the traditional efficacy trial for EBOV vaccine is challenging especially long-term evaluation. However current technological advances have resulted in mitigating some of these challenges. Series of mathematical models have been utilized for studying vaccine response especially understanding long-term vaccine-elicited antibodies. Xu., *et al*. developed a novel mathematical model that simulates the dynamics of antibody level after vaccination. By carrying comparative evaluation of antibody dynamics after the administration of series of commonly used vaccines, they reported that booster dosage were

essential in enhancing IgG antibody levels [57]. A previous study by Xu., *et al.* in which they developed a reliable mathematical platform that was used to quantitatively explain the kinetic characteristics of antibody-SARS-CoV-2 interaction which gave a good understanding of antibody and virus dynamics. This platform was therefore essential in predicting the protection period of SARS-CoV-2 antibodies [58]. The importance of mathematical modelling in analysing vaccine response has being outlined by other researchers in studies involving COVID-19 [59-61]. Mathematical modelling is useful when data are scares as it can be used in estimating the duration of response through utilization of additional information based on vaccine mechanism of action and other biological parameters [55].

However, most of these models focus on antibody concentrations that have declined after peak response. Ordinary differential equations (ODEs) are used to humoral immune response in EBOV vaccination. This model can be used in evaluating the dynamics of antibody response in two populations associated with antibody-secreting cells: short-lived and long-lived.

## Conclusion

Evaluation of EBOV vaccine efficacy is a daunting task due to ethical consideration and the sporadic prospective of EBOV outbreaks. Identifying markers of vaccine correlation during EBOV outbreaks would go a long way to measure the efficacy of any vaccines regimen used in such an outbreak. Biomarkers of EBOV vaccine would not only be useful in measuring correlation of protection but would also be useful in understanding how an outbreak is been controlled. During the West Africa outbreak one of the challenges faced by the response team understanding protection correlation especially trying to identify immunological responses to the deployed vaccine, with suggestion that protection correlation of all the EBOV vaccines are not universal [68]. This means when designing a novel biomarker of EBOV vaccine, the prospect of developing a universal biomarker should be a priority.

## Conflict of Interest

Authors do not have any conflict of interest to declare.

## Use of AI and AI-Assisted Technology

Authors declare that they did not use any aspect of AI and AI-assisted technology during preparation of this article.

## Bibliography

1. Malvy D., *et al*. "Ebola virus disease". *The Lancet* 393.10174 (2019): 936-948.
2. Bukreyev AA., *et al*. "Discussions and decisions of the 2012-2014 International Committee on Taxonomy of Viruses (ICTV) Filoviridae Study Group, January 2012-June 2013". *Archives of Virology* 159.4 (2013): 821-830.
3. Bosa HK., *et al*. "The west Africa Ebola virus disease outbreak: 10 years on". *The Lancet* 12.7 (2024): e1081-e1083.
4. Leligdowicz A., *et al*. "Ebola virus disease and critical illness". *Critical Care* 20.1 (2016): 217.
5. Mupapa K., *et al*. "Ebola hemorrhagic fever and pregnancy". *Journal of Infectious Diseases* 179.1 (1999): S11-S12.
6. Rajek A., *et al*. "Insights from clinical research completed during the west Africa Ebola virus disease epidemic". *Lancet Infectious Diseases* 17.9 (2017): e280-e292.
7. Ramharter M and Gunther S. "Evaluating case definitions for Ebola virus disease". *Lancet Infectious Diseases* 20.11 (2020): 1224-1226.
8. Caleo G., *et al*. "Clinical and epidemiological performance of WHO Ebola case definitions: a systematic review and meta-analysis". *Lancet Infectious Diseases* 20.11 (2020): 1324-1338.

9. Martin P., *et al*. "Laboratory diagnosis of Ebola virus disease". *Intensive Care Medicine* 41.5 (2015): 895-898.

10. WHO. "Clinical management of patients with viral hemorrhagic fever: a pocket guide for the front-line health workers". Geneva, Switzerland WHO (2014).

11. Tomori O and Kolawole MO. "Ebola virus disease: current vaccine solutions". *Current Opinion in Immunology* 71 (2021): 27-33.

12. Falzarano D., *et al*. "Progress in filovirus vaccine development: evaluating the potential for clinical use". *Expert Review of Vaccines* 10.1 (2011): 63-77.

13. Clark DK., *et al*. "Safety and immunogenicity of a highly attenuated rVSVN4CTs-EBOVGP1 Ebola virus vaccine: a randomized, double-blind, placebo-controlled, phase 1 clinical trial". *Lancet Infectious Diseases* 20.4 (2020): 455-466.

14. Henoa-Restrepo AM., *et al*. "Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: interim results from the Guinea ring vaccination, open-label, cluster-randomised trial". *Lancet* 386.9996 (2015): 857-866.

15. Henao-Restrepo AM., *et al*. "Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised train". *Lancet* 389.10068 (2017): 505-518.

16. Regules JA., *et al*. "A recombinant vesicular stomatitis virus Ebola vaccine". *New England Journal of Medicine* 376.4 (2017): 330-341.

17. Feldmann H., *et al*. "Ebola: Lessons on vaccine development". *Annual Review of Microbiology* 72 (2018): 423-446.

18. Woolsey C and Geisbert TW. "Current state of Ebola virus vaccines: A snapshot". *PLoS Pathogen* 17.12 (2021): e1010078.

19. Ebola Vaccine Team B, Wellcome Trust, CIDRAP. "Completing the Development of Ebola vaccine: current status, Remaining challenges, and Recommendations" (2017).

20. Custers J., *et al*. "Vaccine based on replication incompetent Ad26 viral vectors: Standardized template with key considerations for a risk/benefit assessment". *Vaccine* 39.22 (2021): 3081-3091.

21. Milligen ID., *et al*. "Safety and immunogenicity of novel adenovirus type 26-modified vaccinia Ankara-vectored ebola vaccines: a randomised clinical trial". *Journal of the American Medical Association* 315.15 (2016): 1610-1623.

22. Ewer K., *et al*. "A monovalent chimpanzee adenovirus Ebola vaccine boosted with MVA". *New England Journal of Medicine* 374.17 (2016): 1635-1646.

23. Tapia MD., *et al*. "Use of ChAd3-EBO-Z virus vaccine in Malian and US adults, and boosting of Malain adults with MVA-BN-Filo: a phase 1, single-blind, randomised trail, a phase 1b, open-label and double-blind, dose-escalation trial, and a nested, randomised, double-blind, placebo-controlled trial". *Lancet Infectious Diseases* 16.1 (2016): 31-42.

24. Dolzhikova IV., *et al*. "Safety and immunogenicity of GamEvac-Combi, a heterologous VSV- and Ad5- vectored Ebola vaccine: An open phase I/II trial in healthy adults in Russia". *Human Vaccines and Immunotherapeutics* 13.3 (2017): 613-620.

25. Matunvanga TZ., *et al*. "Setting-up an Ebola vaccine trial in a remote area of the Democratic Republic of Congo: challenges, mitigation, and lessons learned". *Vaccine* 40.25 (2022): 3470-3480.

26. Lariviere Y., *et al*. "Open-label, randomised, clinical trial to evaluate the immunogenicity and safety of a prophylactic vaccination of healthcare providers by administration of a heterologous vaccine regimen against Ebola in the Democratic Republic of the Congo: the study protocol". *BMJ Open* 11.9 (2021): e046835.

27. Pollard AJ., *et al*. "Safety and immunogenicity of a two-dose heterologus Ad26.ZEBOV and MVA-BN-Filo Ebola vaccine regimen in adults in Europe (EBOVAC2) a randomised, observer-blind, participant-blind, placebo-controlled, phase 2 trial". *Lancet Infectious Diseases* 21.4 (2021): 493-506.

28. Kibuuka H., *et al*. "Safety and immunogenicity of Ebola virus and Marburg virus glycoprotein DNA vaccines assessed separately and concomitantly in healthy Ugandan adults: a phase 1b, randomized, double-blind, placebo-controlled clinical trial". *Lancet* 385.9977 (2015): 1545-1554.

29. Li J-X., *et al*. "Immunity duration of a recombinant adenovirus type-5 vector-based Ebola vaccine and a homologous prime-boost immunisation in healthy adults in China: final report of a randomised, double-blind, placebo-controlled, phase 1 trial". *Lancet Global Health* 5.3 (2017): e324-e334.

30. Zhu F-C, Hou LH., *et al*. "Safety and immunogenicity of a novel recombinant adenovirus type-5 vector-based Ebola vaccine in healthy adults in China: preliminary report of a randomized, double-blind, placebo-controlled, phase 1 trial". *Lancet* 385.9984 (2015): 2272-2279.

31. Ishola D., *et al*. "Safety and long-term immunogenicity of the two-dose heterologous Ad26.ZEBOV and MVA-BN-Filo Ebola vaccine regimen in adults in Sierra Leone: a combined open-label, non-randomised stage 1, and a randomised, double-blind, controlled stage 2 trial". *Lancet Infectious Diseases* 22.1 (2022): 97-109.

32. Afolabi MO., *et al*. "Safety and immunogenicity of the two-dose heterologous Ad26.ZEBOV and MVA-BN-Filo Ebola vaccine regimen in children in Sierra Leone: a randomised, double-blind, controlled trial". *Lancet Infectious Diseases* 22.1 (2022): 110-122.

33. Mooney T., *et al*. "EBOVAC-Salone: Lessons learned from implementing an Ebola vaccine trial in an Ebola-affected country". *Clinical Trials* 15.5 (2018): 436-443.

34. Van Thilbeurgh M., *et al*. "Predictive markers of immunogenicity and efficacy for human vaccines". *Vaccines* 9.6 (2021): 579.

35. Aronson JK. "Research priorities in biomarkers and surrogate end-points". *British Journal of Clinical Pharmacology* 73.6 (2012): 900-907.

36. Zhu Y., *et al*. "Toward the development of monoclonal antibody-based assays to probe virion-like epitopes in hepatitis B vaccine antigen". *Human Vaccines and Immunotherapeutics* 10.4 (2014): 1013-1023.

37. Huang Y., *et al*. "Simultaneous evaluation of the magnitude and breadth of a left and right censored multivariate response, with application to HIV vaccine development". *Statistics in Biopharmaceutical Research* 1.1 (2009): 81-91.

38. Poestsch JH., *et al*. "Detectable Vesicular Stomatitis virus (VSV)-specific humoral and cellular immune responses following VSV-Ebola Virus vaccination". *Journal of Infectious Diseases* 219.4 (2019): 556-561.

39. Van Tilbeurgh M., *et al*. "Predictive markers of immunogenicity and efficacy for human vaccines". *Vaccines (Basel)* 9.6 (2021): 579.

40. DeGottardi Q., *et al*. "Ontogeny of different subsets of yellow fever virus-specific circulatory CXCR+ CD4+ T cell after yellow fever vaccination". *Scientific Reports* 10.1 (2020): 15686.

41. Baloh CH., *et al*. "Biomarkers detected in cord blood predict vaccine responses in young infants". *Frontiers in Immunology* 14 (2023): 1152538.

42. Weinberg A., *et al*. "Varicella-Zoster virus-specific immune responses to Herpes Zoster in elderly participants in a trial of the clinically effective Zoster vaccine". *Journal of Infectious Diseases* 200.7 (2009): 1068-1077.

43. Moss B. "Smallpox vaccines: targets of protective immunity". *Immunological Review* 239.1 (2011): S8-S26.

44. Julkunen I., *et al*. "Antibody responses to mumps virus proteins in natural mumps infection and after vaccination with live and inactivated mumps virus vaccines". *Journal of Medical Virology* 14.3 (1984): 209-219.

45. Monath TP. "Yellow fever: an update". *Lancet Infectious Diseases* 1.1 (2001): P11-P20.

46. Darrah PA., *et al*. "Prevention of tuberculosis in macaques after intravenous BCG immunization". *Nature* 577 (2020): 95-102.

47. Pattyn J., *et al*. "Infection and vaccine-induced HPV-specific antibodies in cervicovaginal secretions. A review of the literature". *Papillomavirus Research* 8 (2019): 100185.

48. Rivera A and Messaoudi I. "Molecular mechanisms of Ebola pathogenesis". *Journal of Leukocyte Biology* 100.5 (2016): 889-904.

49. Follman D. "Augmented designs to assess immune response in vaccine trials". *Biometric* 62.4 (2006): 1161-1169.

50. Apostolopoulos V and Marincola FM. "Methods to measure vaccine immunity". *Expert Review of Vaccines* 9.6 (2010): 545-546.

51. Bannister S., *et al*. "The emerging role of epigenetic in the immune response to vaccination and infection: a systematic review". *Epigenetic* 15.6-7 (2020): 555-593.

52. Haq K and EmElhaney JE. "Immunosenescence: influenza vaccination and the elderly". *Current Opinion in Immunology* 29 (2014): 38-42.

53. Gensous N., *et al*. "Responders and non-responders to influenza vaccination: A DNA methylation approach on blood cells". *Experimental Gerontology* 105 (2018): 94-100.

54. Plotkin SA and Gilbert PB. "Nomenclature for immune correlates of protection after vaccination". *Clinical Infectious Diseases* 54.11 (2012): 1615-1617.

55. Alexandre M., *et al*. "Prediction of long-term humoral response induced by the two-dose heterologous Ad26.ZEBOV, MVA-BN-Filo vaccine against Ebola". *NPJ Vaccine* 8.1 (2023): 174.

56. Roozendaal R., *et al*. "Nonhuman primate to human innunobridging to infer the protective effect of an Ebola virus vaccine candidate". *NPJ Vaccine* 5.1 (2020): 112.

57. Xu Z., *et al*. "A mathematical model simulating the adaptive immune response in various vaccines and vaccination strategies". *Scientific Reports* 14.1 (2024): 23995.

58. Xu Z., *et al*. "A novel mathematical model that predicts the protection time of SARS-CoV-2 antibodies". *Viruses* 15.2 (2023): 586.

59. Nakamura N., *et al*. "Modeling and predicting individual variation in COVID-19 vaccine-elicited antibody response in the general population". *PLOS Digital Health* 3.5 (2024): e0000497.

60. De Pillis L., *et al*. "A mathematical model of the within-host kinetics of SARS-CoV-2 neutralizing antibodies following COVID-19 vaccination". *Journal of Theoretical Biology* 556 (2023): 111280.

61. Russell TW., *et al*. "Real-time estimation of immunological response against emerging SARS-CoV-2 variants in the UK: a mathematical modelling study". *Lancet Infectious Diseases* 25.1 (2025): P80-P93.

62. De Santis O., *et al*. "Safety and immunogenicity of a chimpanzee adenovirus-vectored Ebola vaccine in healthy adults: a randomised, double-blind, placebo-controlled, dose-finding, phase 1/2a study". *Lancet Infectious Diseases* 16.3 (2016): 311-320.

63. Lambe T., *et al*. "Detection of vaccine-induced antibodies to Ebola virus in oral fluid". *Open Forum Infectious Diseases* 3.1 (2016): ofw031.

64. Ewer K., *et al*. "A monovalent chimpanzee adenovirus Ebola vaccine boosted with MVA". *New England Journal of Medicine* 374.17 (2016): 1635-1640.

65. Milligan ID., *et al*. "Safety and immunogenicity of novel adenovirus type 26- and modified vaccinia Ankara-vectored Ebola vaccines: A randomized clinical trial". *Journal of the American Medical Association* 315.15 (2016): 1610-1623.

66. Winslow RL., *et al*. "Immune responses to novel adenovirus type 26 and modified vaccinia virus Ankara-vectored Ebola vaccines at 1 year". *Journal of the American Medical Association* 317.10 (2017): 1075-1077.

67. Rechtien A., *et al*. "Systems vaccinology identifies an early innate immune signature as a correlate of antibody responses to the Ebola vaccine rVSV-ZEBOV". *Cell Reports* 20.9 (2017): 2251-2261.

68. Meyer M., *et al*. "Can Ebola Virus vaccine have a universal immune correlates of protection?" *Trends in Microbiology* 27.1 (2019): 8-16.

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