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# Bundibugyo virus vaccine landscape and data regarding cross protection

22 May 2026

1

## Evidence and readiness ranking of vaccine candidates with potential for BDBV cross-protection

| Vaccine/Platform & company/university | Cross reactivity/ cross –protection evidence | Key references | Readiness | BDBV relevance |
|---|---|---|---|---|
| Erbevo (rVSV-EBOV) (Merck) | • Partial protection against BDBV challenge in macaque model with lab derived material (3 of 4 rVSV-EBOV vs 1 of 4 neg control). Not sterile protection – animals had viremia and were symptomatic<br>• Lab derived rVSV EBOV and rVSV SUDV co-administered, provided no protection (1/3) .<br>• Antibodies reactive to BDBV GP in 6 Erbevo vaccine recipients from a Phase I study; cross-reactive mAbs also isolated from these samples | Falzarano et al 2011<br>Mire et al 2013<br>Ehrhardt et al 2019 | Licensed (WHO-prequalified) for EBOV;<br>Doses available | Erbevo elicits antibody responses of unknown protective effect to BDBV and conflicting data related to partial protection in NHP model |
| rVSV prime boost (rVSV-SUDV GP+ rVSV-EBOV GP) (UTMB – Tom Geisbert) | • Heterologous rVSV prime–boost strategies using SUDV followed by a boost with EBOV showed improved protection against BDBV in macaques (3/3)<br>• In both groups, numbers were small and lab produced material was used. | Mire et al 2013 | Erbevo Licensed (WHO-prequalified;<br>Doses available IAVI SUDV clinical doses available | A prime boost regimen gave increased protection against BDBV, but no clinical experience with this regimen; direct mixture not protective |
| Zabdeno (Ad26.ZEBOV) / Mvabea (MVA-BN-Filo (J&J) | • No animal model data for BDBV<br>• One study of samples from vaccine recipients - low or absent ELISA or neut titers against Bundibugyo. | Mdluli et al 2025 | Licensed (WHO-prequalified) for EBOV; withdrawn EMA; Unclear if doses available | No evidence for strong BDBV cross reactivity or protection |

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2

# Evidence and readiness ranking of vaccine candidates with potential for BDBV cross-protection

| Vaccine/Platform & company/university | Cross reactivity/ cross –protection evidence | Key references | Readiness | BDBV relevance |
|---|---|---|---|---|
| ChAdOx1 bivalent (EBOV/SUDV) (Oxford – Tess Lambe) | • No published data on BDBV immunogenicity or protection in humans or animal models; published data on lack of SUDV protection in NHPs | N/A | Phase I; Doses available | No evidence for BDBV cross reactivity or protection |
| ChAd3 SUDV GP (Sabin) | • No published data on BDBV immunogenicity or protection in humans or animal models; Potential for cross reactivity, | N/A | Phase II; Doses available | No evidence for BDBV cross reactivity or protection |
| rVSV-SUDV GP (IAVI ) | • No published data on BDBV immunogenicity or protection in humans or animal models; Potential for cross reactivity, | N/A | Phase I: doses available | No evidence for BDBV cross reactivity or protection |

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3

# Bundibugyo-specific vaccine candidates

| Vaccine/Platform & company/university | Immunogenicity / Efficacy evidence | Key references | Readiness |
|---|---|---|---|
| rVSVΔG -BDBV-GP (UTMB and RML- Tom Geisbert and Andrea Marzi) | • 100% protection in BDBV macaque model (3/3)<br>• Postexposure protection in BDBV Macaque model - 83% (5/6)<br>• Partial protection against EBOV challenge in the EBOV Guinea pig model (1/6) | Mire et al 2011<br>Woolsey et al 2023 (a)<br>Marzi et al 2011 | • No clinical grade vaccine or current manufacturer |
| rVSV-N4CT1 GP tetravalent (Aurovaccines) | • Mixture of VSV expressing either EBOV,SUDV,BDBV,MARV GP protected 100% against all *Ebolavirus* species (6/6 each EBOV, SUDV, BDBV) and 83% against MARV (5/6) | Woolsey et al 2023 (b) | • No clinical grade vaccine; unclear if manufacturer is still engaged<br>• Unclear if the BDBV vaccine alone is efficacious.<br>• Complexity of Quadrivalent |
| HPIV3 Trivalent GP (UTMB – Alex Bukreyev) | • Monovalent HPIV3-BDBVand trivalent HPIV-BDBV/EBOV/SUDV each protect against BDBV challenge (5/5 each group) in ferrets<br>• Other Antibody functions important in protection (delivery is mucosal so other effector mechanisms of immunity in play) | Kimble et al 2019<br>Malherbe et al 2023 | • No clinical grade vaccine or manufacturer<br>• No data in NHPs |
| ChAdOx1 – BDBV GP (Oxford – Tess Lambe) | • No immunogenicity or efficacy data has been generated | Personal communication | • No clinical grade vaccine; Construct can be quickly scaled up<br>• Lack of pre-clinical data |
| mRNA –LNP –BDBV GP (Moderna) | • BDBV construct made but amount of pre-clinical data unclear | Personal communication | • No clinical grade vaccine; Construct can be quickly scaled up<br>• Unclear pre-clinical data |

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4

# Broadly-reactive candidates

| Vaccine/Platform & company/university | Immunogenicity / Efficacy evidence | Key references | Readiness |
|---|---|---|---|
| mRNA –LNP with mixed mRNAs (GP EBOV, SUDV, BDBV + NP EBOV) (Univ Sci.&Tech. China, RNAlfa Biotech) | Broad immunity elicited against EBOV, SUDV and BDBV in mice. Complete protection in EBOV mouse model, in IFNAR KO mouse model for BDBV, and SUDV hamster model with the mixture and some of the individual components | Zhang et al 2026 | Pre-clinical data ; brand new report, full maturity unclear |
| ChAdOx1 + MVA , T cell epitopes from NP, VP40 and L (Oxford – Tomas Hanke) | ChAdOx1 prime and MVA boost elicited broad T cell responses and 100% protection in mice against EBOV and MARV. | Rahim et al 2019 | Pre-clinical data only and lab scale material |
| Glycoprotein Multivalent Vaccines (Protein Subunit plus adjuvant (CPG, MPLA and Addavax) (UC Irvine / U. New Mexico) | Recombinant GP for EBOV, SUDV, BDBV + CPG, MPLA and Addavax elicited broad humoral immunity; moderate neutralizing titers. | Felgner et al 2024 | Pre-clinical data only and lab scale material |
| EBOV/SUDV GPs + Gag-VLPs plus adjuvant (CCHMC/Emory/UNC) | Bivalent EBOV/SUDV GP Gag VLPs induced BDBV ELISA and neut titers in NHPs | Singh et al 2020 | Pre-clinical data only and lab scale material |
| Recombinant modified EBOV, SUDV BDBV GP on nanoparticles (Scripps, Uvax) | Mutliple GP designs for EBOV, SUDV and BDBV expressed and assembled on nanoparticles; mouse immunogenicity of EBOV and SUDV designs elicited BDBV responses in mice | Lee et al 2025 | Pre-clinical data only and lab scale material |

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5

# Broadly-reactive candidates

| Vaccine/Platform & company/university | Immunogenicity / Efficacy evidence | Key references | Readiness |
|---|---|---|---|
| mRNA-LNP; Broadly reactive design GP nanoparticle (Stanford – Peter Kim) | The protein nanoparticle version of the vaccine elicits immune responses (ELISA and psVNA) against EBOV, SUDV and BDBV in mice and guinea pigs (prime + boost regimen). mRNA-LNP vaccine study in progress in guinea pigs | Personal communication | Pre-clinical data only and lab scale material |
| Broadly reactive BDBV GP arrayed on VLP (Adaptvac) | GP antigen designed and arrayed on VLP surface; mouse immunogenicity experiments in progress | Personal communication | Pre-clinical data only and lab scale material |
| Broadly reactive design, GP protein (insect and mammalian) with AHQ-11 or SMNP adjuvant (Abvacc) | GP protein vaccine elicits immune resposnes (ELISA and psVNA) against SUDV, EBOV and BDBV in mice and guinea pigs. (prime + boost) Efficacy data for Ebola in mouse model and for SUDV in guinea pig model. BDBV challenge has not yet been done (prime + boost) | Personal communication | Pre-clinical data only and lab scale material |

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6

## Acknowledgements

- CEPI : Polina Brangel, Tung Thanh Le, John Shannon, Javier Castillo-Olivares
- ANRS: Mélanie Ngyuyen-Marzin, Hérve Raoul, Yazdan Yazdanpanah
- Beth-Ann Coller
- All those who provided unpublished data

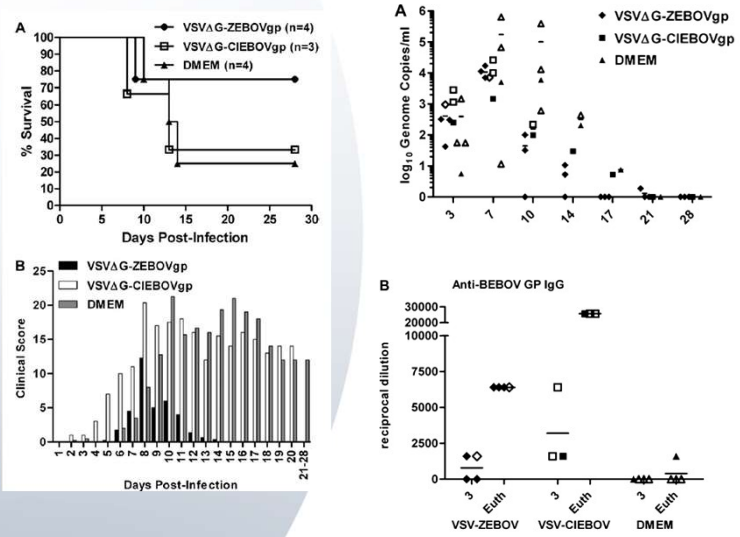

7

# Data slides

8

# VSV-EBOV GP protection in NHPs (Falarzano et al 2011)

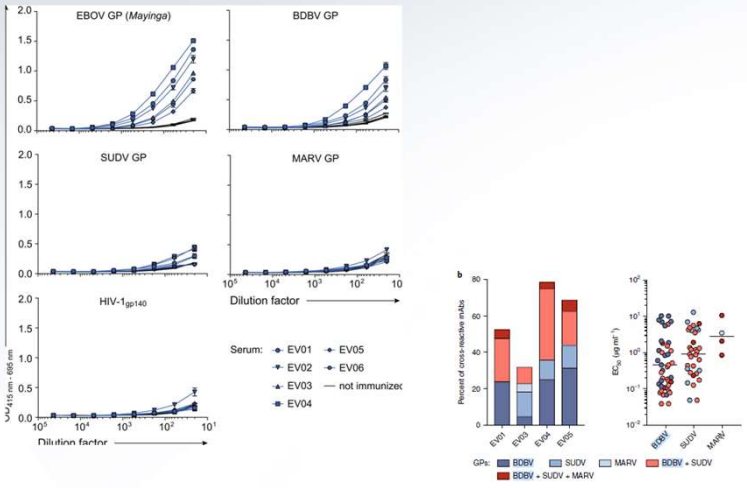
- Partial protection was seen against BDBV from the rVSV-ZEBOV.
- This was not sterilizing protection, as seen from the genome copies present in all animals as well as clinical signs
- Anti-BDBV IgG was present after vaccination at low titers, boosted after infection




9

# BDBV immune resposnes in Erbevo vaccine recipients Ehrhardt et al 2019)

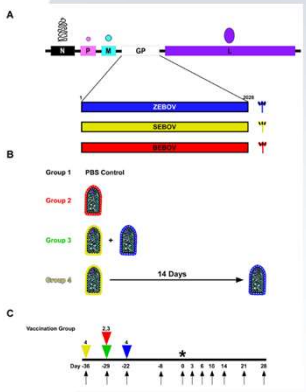
- Anti-GP ELISA with sera from 6 Erbevo vaccinees demonstrates responses against BDBV are present, although reduced compared to EBOV
- Binding analysis of mAbs isolated from Erbevo vaccinees shows many have anti-BDBV binding and neutralizing activity

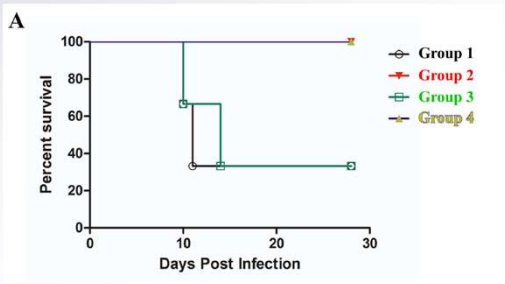



10

# VSV-BDBV GP, VSV-EBOV GP and VSV-SUDV GP protection in NHPs (Mire et al 2013)

- A VSV-BDBV vaccine provided 100% protection in NHPs (3/3)(Group 2)
- A mixture of VSV-EBOV and VSV-SUDV was not effective more than the negative control (0/3)(Group 3)
- Immunizing with VSV-SUDV followed by a VSV-EBOV boost resulted in 100%protection (3/3) (Group 4)

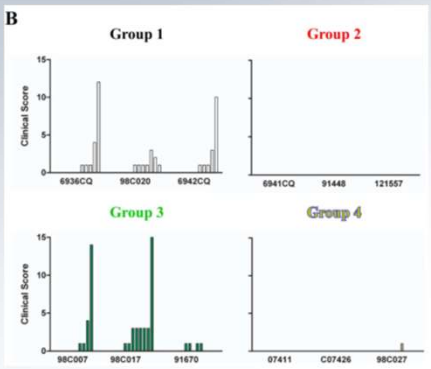


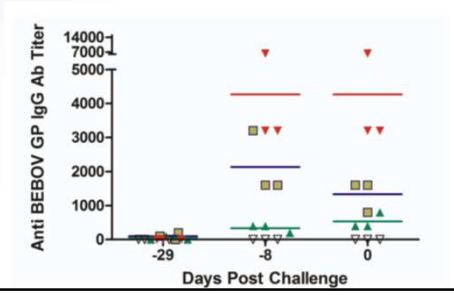




11

# VSV-BDBV GP, VSV-EBOV GP and VSV-SUDV GP protection in NHPs (Mire et al 2013)

- Surviving animals from groups 2 and 4 (VSV-BDBV or VSV-SUDV/ VSV-EBOV prime:boost groups) had no clinical scores and no viremia
- Surviving animal from group 3 (blended VSV-SUDV and VSV-EBOV) had lower clinical score and lower viremia than surviving aniaml from Group 1 and lower
- Group 3 had no or very low binding ab titers and no neutralizing Ab titers pre-challenge

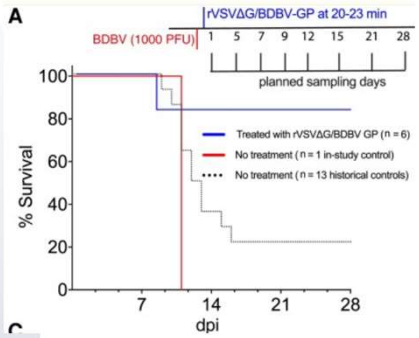


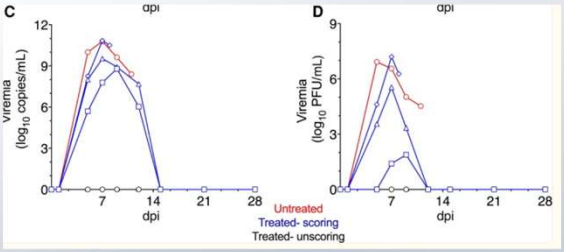




12

# Post exposure protection VSV-BDBV GP (Woolsey et al 2023)

- VSV-BDBV Vaccine administered immediately post exposure protected 5/6 NHPs
- Surviving animals had viremia but were not symptomatic




13

# VSV-BDBV GP Guinea pig study (Marzi et al 2011)

- VSV-BDBV GP vaccine was used to immunize guinea pigs , which were challenged with EBOV
- 1/6 animals survived
- No BDBV challenge performed (lack of model at the time)

**Table 1. Recombinant Vesicular Stomatitis Virus Ebola Virus Glycoprotein Cross-Protective Efficacy in Rodent Models**

| Vaccine | Mice MA-ZEBOV survival (*n* survival/*n* total) | Time to death (d) | Guinea Pigs GPA-ZEBOV Survival (*n* survival/*n* total) | Time to death (d) |
|---|---|---|---|---|
| Control | 4/21 | 6.5 ± 1.5 | 0/6 | 7.3 ± 0.5 |
| rVSV**wt** | 5/21 | 5.6 ± 1.6 | 0/6 | 7.0 ± 0 |
| rVSV-**B-GP** | n.d. | n.a. | 1/6 | 9.4 ± 3.1 |
| rVSV-**Cl-GP** | 22/22 | n.a. | 1/6 | 9.4 ± 2.3 |
| rVSV-**R-GP** | 20/20 | n.a. | 1/6 | 9.2 ± 2.5 |
| rVSV-**S Boniface-GP** | 15/20 | 6.8 ± 0.4 | 0/6 | 7.7 ± 0.5 |
| rVSV-**S Gulu-GP** | n.d. | n.a. | 0/6 | 7.8 ± 0.4 |
| rVSV-**Z Mayinga-GP** | 20/20 | n.a. | 6/6 | n.d. |
| rVSV-**Z Kikwit-GP** | n.a. | n.a. | 4/4 | n.a. |

14

# Back up slides

15

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16

## Key Ranked Interpretation

### 1. ERVEBO (rVSV-ZEBOV) — Highest immediate operational value

- Only *immediately deployable licensed vaccine* with established manufacturing and stockpiles.
- Demonstrates partial heterologous cross-protection in a BDBV NHP model , although only 4 animals
- There are BDBV cross-reactive antibody responses in some Erbevo vaccine recipients (although the numbers are low)
- Confounding data: VSV-EBOV + VSV-SUDV was not effective in an NHP study when administered together, only when administered as a prime:boost regimen.

### 2. Zabdeno/Mvabea (Ad26.ZEBOV / MVA-BN-Filo) — Unlikely relevance for BDBV response

- Designed and optimised for EBOV with a heterologous prime–boost schedule.
- No cross-protective efficacy against BDBV has been demonstrated.
- No longer EMA licensed

### 3. ChAdOx1-based bivalent vaccine —Theoretical but unproven cross-reactivity

- Adenoviral vector platform supports broader antigen presentation and theoretical T-cell mediated cross-reactivity across ebolaviruses.
- However, there is no data for cross reactivity or efficacy against Bundibugyo
- No protection against SUDV in NHPs

### 4. Sabin and IAVI platforms — potential for increased efficacy in a heterologous prime:boost with Erbevo

- rVSV-SUDV prime and rVSV-EBOV boost showed good efficacy in the BDBV NHP model, but this regimen has not been assessed in humans; this would also be pairing the approved vaccine with an investigational product, which would be complex

17

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18