Immunogenicity of rVSVΔG-ZEBOV-GP Ebola Vaccine (ERVEBO®) in African Participants by Age, Sex, and Baseline GP-ELISA Titer: A Post Hoc Analysis of 3 Phase 2/3 Trials

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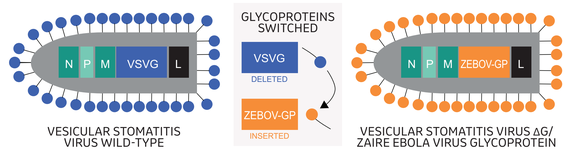
Background

- Ebola virus disease (EVD) is a rare, acute illness with a mortality rate ranging from 25% to 90%[1]
- There is currently no antiviral drug licensed by the U.S. Food and Drug Administration for EVD treatment in people. When used early, basic interventions to treat symptoms may significantly improve the chances of survival[1]
- ERVEBO®, a live recombinant vesicular stomatitis virus (VSV) vaccine containing the *Zaire ebolavirus* glycoprotein (GP) in place of the VSV GP (rVSVΔG-ZEBOV-GP), was developed by Merck & Co., Inc., Kenilworth, NJ, USA, in collaboration with multiple partners to prevent EVD and has been approved for human use in several countries[2]
- rVSVΔG-ZEBOV-GP has been shown to be generally safe and well tolerated, with most adverse events reported as mild to moderate. However, a multivariate analysis identified female sex and medical history of arthritis as potential risk factors for the development of arthritis postvaccination[2,3]
- The objective of this post-hoc analysis was to assess the immunogenicity of rVSVΔG-ZEBOV-GP in subgroups by sex, age, and prior exposure using pooled data from Phase 2/3 clinical trial data

Figure 1. rVSVΔG-ZEBOV-GP, Live Attenuated (ERVEBO®)



VESICULAR STOMATITIS VIRUS WILD-TYPE

VESICULAR STOMATITIS VIRUS ΔG/ ZAIRE EBOLA VIRUS GLYCOPROTEIN

The V920 vaccine (ERVEBO®) is a live, attenuated, recombinant vesicular stomatitis virus (rVSV)-based, chimeric-vector vaccine for which the VSV envelope protein was deleted and replaced (ΔG) by inserting only the envelope glycoprotein (GP) of Zaire ebolavirus (ZEBOV)

There is no live Zaire ebolavirus in the vaccine

Methods

- Data were pooled from 3 Phase 2/3 clinical trials conducted during the 2013-2016 West African outbreak
  - No data from the Ebola ça Suffit efficacy trial were included in this analysis, since samples for immunogenicity were not collected
  - Guinea (Front Line Workers [FLW]) was an open-label, nonrandomized, single-arm safety and immunogenicity evaluation of FLWs, including personnel working in Ebola or non-Ebola health facilities and services[4]
  - Sierra Leone (STRIVE) was a randomized, open-label, Phase 2/3, single-arm trial with phased vaccine introduction, no placebo, and concurrent evaluation of vaccine safety and efficacy in healthcare and front-line response workers[5]
  - Liberia (PREVAIL) was a randomized, placebo-controlled, Phase 2 trial to evaluate safety and immunogenicity of 2 vaccines: ChAd3-EBO-Z and rVSVΔG-ZEBOV-GP in adults[6]
- Assessed immune responses using a validated assay in each of the three studies and performed a post-hoc analysis by:
  - Sex
  - Age (18-50 yr and >50 yr)
  - Baseline (BL) GP-enzyme-linked immunosorbent assay (ELISA) titer (<200 and ≥200 EU/mL)

Statistical Methods

- The full analysis set (FAS) population included the primary immunogenicity populations (all rVSVΔG-ZEBOV-GP-vaccinated participants with serology data collected within an acceptable day range) from all three trials
- Participants with missing or out-of-day-range assays were excluded by time point
- Participants from PREVAIL receiving the ChAd3-EBO-Z vaccine or placebo were not included in the analyses
- Endpoints were immune responses measured at Days 14, 28, 180, and 365 postvaccination:
  - Total IgG antibody response (ELISA units per milliliter [EU/mL]) measured by the GP-ELISA
  - Neutralizing antibody response measured by the plaque reduction neutralization test (PRNT)
- For both the GP-ELISA and PRNT assays, analyses included calculation of GMT at baseline and 14 days (FLW trial only), 28 days, 180 days, and 12 months (PREVAIL and STRIVE trials only) after vaccination
- Seroresponse was defined 2 ways for the GP-ELISA:
  1. ≥200 EU/mL and ≥2-fold increase from baseline, which was the definition that best differentiated vaccine from placebo recipients in the PREVAIL clinical trial[6]
  2. ≥4-fold increase from baseline, which is a frequently used historical definition of seroresponse
- The 95% confidence intervals (CI) for geometric mean titers (GMT) were based on analysis of variance, and the CI for seroresponse was based on the exact binomial method
- For GMTs, all sera with evaluable results were included; however, a baseline evaluable result was required for calculation of seroresponse
- Statistical analyses were conducted in SAS v9.4 (Cary, NC)

Table 1. Population Baseline Characteristics

Participants in Population	N = 2,199
Sex, n (%)	
Male	1,487 (67.6)
Female	712 (32.4)
Age, years, n (%)	
18 to 50	1972 (89.7)
>50	227 (10.3)
Mean (SD)	33.9 (10.9)
Range	18 to 77
Study, n (%)	
FLW	1,217 (55.3)
STRIVE	505 (23.0)
PREVAIL	477 (21.7)
Baseline GP-ELISA, n (%)	
<200	1,812 (82.4)
≥200	278 (12.6)
Missing	109 (5.0)

Figure 2. Geometric Mean Titers Measured by GP-ELISA and PRNT

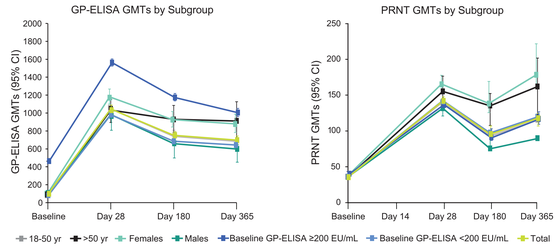


Figure 3. GP-ELISA Seroresponse ≥2-fold Increase From Baseline and ≥200 EU/mL

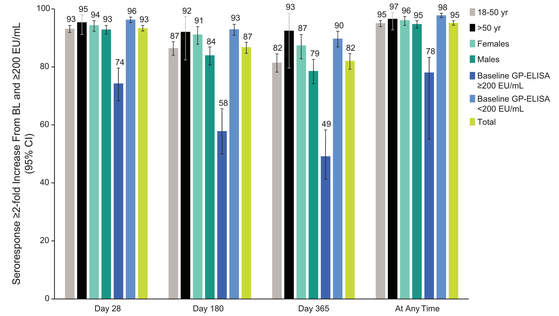


Figure 4. GP-ELISA Seroresponse ≥4-fold Increase From Baseline

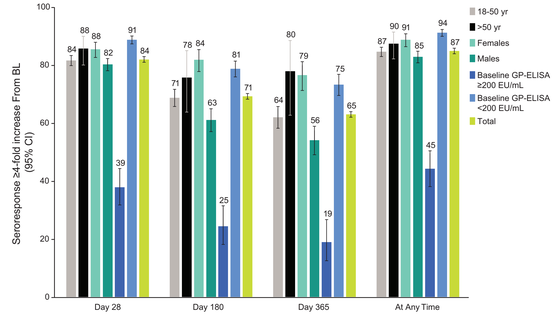
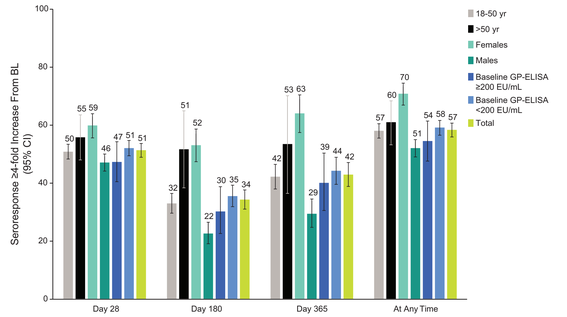


Figure 5. PRNT Seroresponse ≥4-fold Increase From Baseline



Summary

- GP-ELISA and PRNT geometric mean titers increased significantly from baseline, with most peaking at Day 28 and persisting through Day 365 in the total population and in all subgroups
- There were differences in the magnitude of the immune response between men and women and between participants with baseline GP-ELISA <200 and ≥200 EU/mL, although no differences in efficacy have been assessed for these subgroups
- There did not appear to be a difference between age groups in GP-ELISA or PRNT geometric mean titers
- Vaccinees with baseline GP-ELISA ≥200 EU/mL had a reduced GP-ELISA seroresponse, defined as ≥2-fold increase from baseline and ≥200 EU/mL, and ≥4-fold increase from baseline when measured at any time point postvaccination. This is expected since a high-fold increase is harder to achieve when starting at a high baseline, but was not observed when measured using PRNT and defined as ≥4-fold increase from baseline, likely because of the narrower range of the PRNT assay compared with the GP-ELISA
- These data demonstrate that vaccination with rVSVΔG-ZEBOV-GP produces a robust immune response in participants regardless of sex, age, or previous exposure

References

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