

Sierra Leone Trial to Introduce a Vaccine against Ebola (STRIVE)

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Prologue to STRIVE

- West Africa Ebola outbreak unprecedented in size and complexity
- WHO convened consultation on potential Ebola therapies and vaccines (September 2014)
 - “Accelerate [vaccine] development and safe use in countries with outbreaks”
- CDC decided to expand West Africa response to include vaccine trial

STRIVE Overarching Goal and Objectives

Overarching Goal

To accelerate introduction and use of an Ebola prevention vaccine among at-risk people in Sierra Leone with concurrent evaluation of the efficacy and safety of the vaccine

Objectives

- Estimate the efficacy of a single dose of rVSV-ZEBOV preventing laboratory-confirmed Ebola virus disease (EVD)
- Assess serious adverse events (SAE) following administration of the vaccine
- Collect and store serum for baseline seroprevalence and immunogenicity evaluations

STRIVE Principal Study Partners

Sierra Leone

- College of Medicine and Allied Health Sciences (COMAHS)
- Ministry of Health and Sanitation (MOHS)

United States

- CDC
- The Biomedical Advanced Research and Development Authority (BARDA)
- Merck/New Link



The Vaccine: rVSV-ZEBOV

- Live-attenuated recombinant vesicular stomatitis virus (rVSV) vaccine expressing the glycoprotein of Zaire Ebola virus (ZEBOV)
- Developed by Public Health Agency Canada; Merck currently holds license
- Administered as a single dose (2×10^7 pfu/mL)
- Stored -80°C



Study Design

- Unblinded, randomized trial
- Phased enrollment over ~4 months
- Participants individually randomized to:
 - *Immediate group*: vaccinated at/within 7 days enrollment
 - *Deferred group*: vaccinated 18-24 weeks after enrollment
- No placebo – all participants vaccinated by end of study
- Vaccine efficacy measured by comparing EVD incidence in vaccinated and deferred groups
- Adverse events (AE) assessed by following participants post-vaccination

Study Population

- Adults ≥ 18 years old
- Health care workers (Ebola and non-Ebola facilities)
- Defined by working in health care setting, not job
 - Physicians Laboratorians Cleaners
 - Nurses Pharmacists Administrators
 - Health aids “Dressers” Security guards
- Selected Ebola frontline workers
 - Surveillance officers Swabbers
 - Ambulance drivers Burial workers

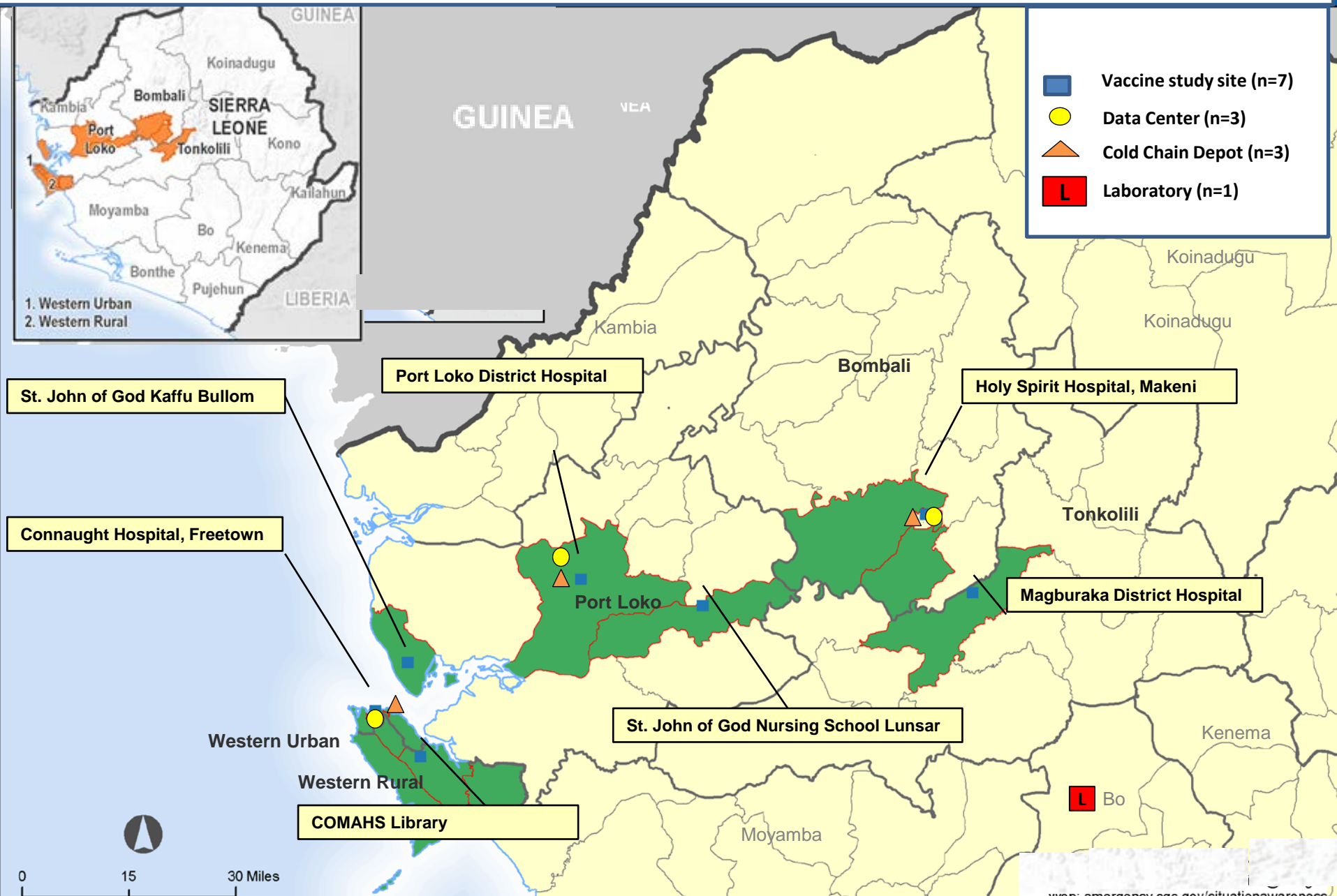


Site Selection

- Sample size considerations – epidemiology early in outbreak
- Logistical considerations
 - Existing infrastructure/ability to enhance infrastructure
 - Buildings, cold chain, roads/transportation
- Ability to monitor for/ensure standard of care for AEs and EVD



STRIVE Study Sites, Sierra Leone



Participant Follow-up

- Monitored for AE, SAE, EVD, pregnancy
 - *Vaccinated group* – 6 months post-vaccination
 - *Deferred group* – From enrollment until vaccinated; then 6 months
- Monthly phone calls; home visits if cannot be contacted
- Evaluation of all SAEs by study physician
- Surveillance to identify participants with suspect EVD admitted to EHC/ETU/hospital isolation units



Safety and Immunogenicity Sub-studies

Safety sub-study

- Intensive safety and reactogenicity assessment
- 400+ initial participants (~200 immediate, ~200 deferred)
- Filled out daily health cards day 1-28
- Followed-up by phone days 1,3, 7,14, 28

Immunogenicity sub-study (n~500)

- In collaboration with Merck
- Baseline seroprevalence and long-term immunogenicity
- Specimens drawn at 0 (pre-vax), 1, 6, 12-months post-vax
- Tested in US by Merck/Focus Diagnostics

High-Level Results*

- Enrollment complete: 8,680 enrolled (April 9-August 21, 2015)
- As of Oct 18, >5,550 participants vaccinated
 - Immediate vaccination complete: 4,173 vaccinated
 - Deferred vaccination ongoing: >1,350 vaccinated
- Deferred vaccination planned to be finished mid-December
- Safety profile consistent with other published studies
 - No safety signals in sub-study
 - No vaccine-related SAEs
 - 8 deaths reported to date; none vaccine-related (estimate 43 deaths during study)

* Preliminary data through Oct 18, 2015; data subject to change

High-Level Results (cont)*

EVD surveillance

- 43 participants evaluated for suspected EVD
- All EVD negative
- 19 malaria positive (RDT, ICT, smear); 6 additional with clinically-dx malaria

Immunogenicity sub-study

- Enrollment complete (n=506)
- 92% follow-up on eligible 1-month blood draws
- 6-month blood draws commence December 2015

* Preliminary data through Oct 18, 2015; data subject to change

WHO Guinea Ring Vaccination Trial

- Interim results from WHO Guinea ring trial published in Lancet (July 29, 2015)
- Cluster-randomized ring vaccination with rVSV-ZEBOV around contacts and contacts of contacts of index case
 - Immediate vaccination
 - Delayed vaccination (21 days after randomization)
 - Primary outcome lab-confirmed EVD ≥ 10 days after randomization
- Interim analysis included 90 rings (48 immediate, 42 delayed)
- Concluded VSV-ZEBOV “might be highly efficacious” and “most likely effective at the population level when delivered during an EVD outbreak via a ring vaccination strategy”
- Await publication of final results

STRIVE Mid-course Changes

- Based on interim results from Guinea, WHO ring trial expanded into Sierra Leone
 - No randomization - all rings immediately vaccinated
 - To date, two rings vaccinated in Sierra Leone
- Amended STRIVE protocol for early vaccination of deferred participants not-yet-vaccinated if considered to be at higher risk of exposure to EVD
- Ebola case reported in STRIVE district (Sept 2015)
 - Treated in primary health unit and ETU, and lived in community where enrolled STRIVE participants (deferred, not-yet-vaccinated) worked/lived
 - Activated amendment
 - Vaccinated early ~100 deferred participants

STRIVE Mid-course Re-evaluation

- Changing epi of Ebola in Sierra Leone assessment vaccine efficacy unlikely
- Low incidence EVD; little likelihood of exposure
 - 145 reported Ebola cases in Sierra Leone since study commenced*
 - Few reported cases in HCWs
- Expansion of WHO ring trial to Sierra Leone further decreased likelihood of exposure
- STRIVE continues with important safety and immunogenicity data

* WHO sit rep (April 9 – October 14, 2015)

Ebola Vaccines in Phase II/III Clinical Trials in West Africa

rVSV-ZEBOV (Merck/NewLink/PHAC)	STRIVE (CDC) - Sierra Leone PREVAIL (NIH) - Liberia Ca Sufit (WHO) - Guinea +SL FLW (MSF) - Guinea	Phase II; HCW, FLW Phase II; Comparison ChAd3 and placebo Phase III; Ring vax Phase II; HCW, FLW
ChAd3-ZEBOV (NIAID/GSK)	PREVAIL (NIH) - Liberia	Phase II; Comparison rVSV and placebo
Ad26-EBOV/MVA-EBOV (J&J/BN)	Sierra Leone (J+J)	Phase I/II Adults, adol, children Includes CMI
Ad5-EBOV vaccine (China)	Sierra Leone	Phase II Adults

Potential Strategies for Use of Ebola Vaccines

Outbreak control

Ring vaccination
Other?

High-risk groups

Health care workers
Ebola frontline workers
Lab workers
Other?

Is there a role for vaccination around survivors?

Is there a role for vaccination of the general community?



Scientific and Regulatory Considerations for Use of Ebola Vaccines

- Long-term protection from vaccination
 - Relevant for vaccinating HCW/frontline workers/lab staff
 - Applies to affected countries and international responders
- Vaccine use in special populations: children, pregnant women, HIV-infected persons
- Use of vaccine for post-exposure prophylaxis
- Regulatory
 - Current use under IND (clinical trial or expanded access)
 - EUA(FDA) /EUAL(WHO) increase flexibility and ease of use
 - Full licensure most flexible

Making Decisions about the Use of Ebola Vaccine: Ebola Vaccine Advisory Groups

Global Ebola Vaccine Implementation Team (GEVIT)

- WHO (lead), CDC, UNICEF, GAVI, Gates
- Collaborative planning for the introduction of Ebola vaccines

WHO/SAGE

- Working group on Ebola vaccines and vaccination formed Nov 2014
- Developed framework for use of Ebola vaccines
- Presented to SAGE (Oct 20, 2015)

ACIP

- Future Ebola vaccine working group?

STRIVE Successes

- Providing an opportunity to vaccinate >8,500 health care and front line workers; to date have vaccinated >5,550
- Trained ~400 Sierra Leonean staff
- Accumulating safety and immunogenicity data for vaccine licensure
- Increasing research and response capacity in country
- Developing platform for future vaccine and infectious disease research



the **ROAD** to **ZERO**

CDC'S RESPONSE TO THE
West African Ebola Epidemic



2014-2015



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention