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

Susan Goldstein, MD
National Center for Immunizations and Respiratory Diseases
On behalf of the STRIVE Team
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 x $10^7$ 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
  - Nurses
  - Health aids
  - Laboratorians
  - Pharmacists
  - “Dressers”
  - Cleaners
  - Administrators
  - Security guards
- Selected Ebola frontline workers
  - Surveillance officers
  - Ambulance drivers
  - Swabbers
  - 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

- Koinadugu
  - Vaccine study site (n=7)
  - Data Center (n=3)
  - Cold Chain Depot (n=3)
  - Laboratory (n=1)

- Moyamba
  - St. John of God Nursing School Lunsar

- Western Urban
  - Connaught Hospital, Freetown

- Western Rural
  - COMAHS Library

- Bombali
  - Holy Spirit Hospital, Makeni

- Port Loko
  - Port Loko District Hospital
  - Magburaka District Hospital
  - St. John of God Nursing School Lunsar

- Tonkolili

- Kambia

- Connaught Hospital, Freetown

- Koinadugu
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

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Phase(s)</th>
<th>Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>rVSV-ZEBOV (Merck/NewLink/PHAC)</td>
<td>Phase II; HCW, FLW, PREVAIL (NIH) - Liberia, Ca Sufit (WHO) - Guinea + SL, FLW (MSF) - Guinea</td>
<td>Phase II: Comparison ChAd3 and placebo, Phase III: Ring vax</td>
</tr>
<tr>
<td>ChAd3-ZEBOV (NIAID/GSK)</td>
<td>Phase II; Comparison rVSVV and placebo</td>
<td>PREVAIL (NIH) - Liberia</td>
</tr>
<tr>
<td>Ad26-EBOV/MVA-EBOV (J&amp;J/BN)</td>
<td>Phase I/II; Adults, ado, children, Includes CMI</td>
<td>Sierra Leone (J+J)</td>
</tr>
<tr>
<td>Ad5-EBOV vaccine (China)</td>
<td>Phase II</td>
<td>Sierra Leone</td>
</tr>
</tbody>
</table>

**Note:** HCW = Health Care Workers, FLW = Front Line Workers
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