What's coming in adult vaccines and vaccinations?

Ebola vaccine update

Barbara Mahon, MD, MPH
CDC Lead, Sierra Leone Trial to Introduce a Vaccine against Ebola (STRIVE)

National Adult and Influenza Immunization Summit
May 10, 2017

West Africa Ebola epidemic

- December 2013: likely date of first case in Guinea
- March 2014: first cases reported from Guinea
- August 2014: WHO declared a Public Health Emergency of International Concern

28,616 reported cases
11,310 reported deaths
>10,000 survivors

- May 2016: last case in Liberia from “flare up” in Guinea
Prologue to Ebola vaccine trials

- September 2014: WHO consultation on potential Ebola therapies and vaccines
- Participants concluded there was urgent need to
  - “accelerate [vaccine] development and safe use in countries with outbreaks”
  - “[mount] a coordinated effort by the international community to remove unnecessary obstacles”
- Several candidate vaccines had undergone successful preclinical testing
- Multiple organizations began planning clinical trials
Ebola vaccines tested in phase 2/3 trials in West Africa

- Vesicular stomatitis virus vector
  - rVSV-ZEBOV (manufacturer: Merck/NewLink/Public Health Agency of Canada)
- Chimpanzee adenovirus 3 vector
  - ChAd3-ZEBOV (manufacturer: NIAID/GlaxoSmithKline)
- Human adenovirus 26 and modified vaccinia Ankara vectors
  - Ad26-EBOV/MVA-BN-Filo (manufacturer: Johnson & Johnson, Bavarian Nordic)
- Human adenovirus 5 vector
  - Ad5-EBOV (Tianjin CanSino Biotechnology/Beijing Institute of Technology)

rVSV-ZEBOV-GP

- Live-attenuated recombinant vesicular stomatitis virus (rVSV)
- Replication-competent
- Expresses the glycoprotein of Zaire Ebola virus (ZEBOV)

- Good preclinical record
- Single dose, $2 \times 10^7$ pfu
- Storage at $\leq -60^\circ C$
Phase 1 trials of rVSV-ZEBOV-GP

- Conducted in Gabon, Kenya, Hamburg, Geneva, USA
- Common adverse events
  - Injection site pain
  - Fever
  - Headache
  - Myalgia
  - Fatigue
- Arthritis signal

Regules JA, N Engl J Med 2017

WHO-sponsored Ebola ça Suffit! trial
“Guinea ring trial”

- Cluster-randomized trial design
- Clusters randomized to immediate or delayed (21 days) vaccination
- 1° outcome laboratory-confirmed Ebola ≥10 days after randomization

Henao-Restrepo AM et al, Lancet. 2015
Vaccine efficacy
Ebola ça Suffit trial

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of individuals (clusters)</th>
<th>Cases of Ebola virus disease (clusters affected)</th>
<th>Attack rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>2108 (51)</td>
<td>0 (0)</td>
<td>0%</td>
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<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Group B</td>
<td>3075 (47)</td>
<td>16 (7)</td>
<td>0.52%</td>
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Vaccine efficacy:

- 300% (95% CI: 68.5 to 100.0)
- p-value: 0.0045

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

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.

Sierra Leone Trial to Introduce a Vaccine Against Ebola (STRIVE)
STRIVE design
individually randomized, unblinded trial

- Participants individually randomized to:
  - *Immediate vaccination*: at enrollment (or within 7 days)
  - *Deferred vaccination*: 18-24 weeks later
- **Vaccine efficacy**: compare Ebola incidence in vaccinated (immediate) to unvaccinated (deferred)
- **Adverse events**: follow participants for 6 months after enrollment/vaccination
- **Two sub-studies**:
  - Reactogenicity/safety: solicited, unsolicited adverse events for 28 days
  - Immunogenicity: 0, 1, 6, 9-12 months

STRIVE study population:
healthcare and Ebola front line workers

- Ebola incidence in healthcare workers in Sierra Leone ~100 times greater than general population*

*MMWR 2014, 63:1168-1171
STRIVE high-level results

- **Enrollment and vaccination**
  - Enrolled 8,673 participants (April 9 - August 21, 2015)
  - Vaccinated 7,987

- **Safety profile**
  - Safety/reactogenicity profile consistent with published studies
  - No vaccine-related serious adverse events
  - 25 deaths reported in study population—none vaccine-related
    - ~43 expected in study population, based on WHO mortality data

- **Immunogenicity sub-study (n=506)**
  - 0, 1, 6, and 9-12 months specimens collected
  - Assay validated, testing ongoing

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*Data are preliminary and results subject to change

1 Agnandji ST. NEJM 2015; Regules JA. NEJM 2015; Huttner A. Lancet 2015; Henao-Restrepo AM Lancet 2016; Regules NEJM 2017

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**STRIVE safety/reactogenicity: 0-7 days**

% of participants with solicited adverse events

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*Data are preliminary and results subject to change

2 * denotes p-value <0.05
STRIVE safety/reactogenicity: 0-28 days
daily number of solicited adverse events for each participant¹

¹Data are preliminary and results subject to change

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PREVAIL I: Final Protocol

Informed Consent
18+ Years of Age
N = 1,500

VSVΔG-ZEBOV Vaccine
(1 mL) New Link/Merck
N = 500

Saline Placebo
(1 mL)
N = 250

ChAd3-EBO Z Vaccine
(2 mL) GSK
N = 500

Saline Placebo
(2 mL)
N = 250

Antibody testing at Vaccination, Week 1, Month 1, Month 6 and Month 12; also visits at Months 2, 4, 8, and 10. Week 2 visit for 306 participants. Day 3, 10 and 14 blood draws for VSV viral RNA for 24 participants.

Vaccinations for the phase 2 substudy began on February 2 and ended on April 30, 2015; follow-up ended in May 2016. An amendment was then been approved for long-term follow-up.

Slide courtesy of Rick Davey, NIAID
**Geometric Mean Titers Following Vaccination**

- **rVSV-ZEBOV-GP**
  - Immediate ring vaccination for subsequent cases
  - >1500 vaccinated in response to cluster in 3-4/16

- **Adjunct to contact tracing, early detection, isolation**
- **No randomization**—vaccination offered to all eligible persons
- **rVSV-ZEBOV** not licensed, so ring responses under research protocols
- **As of today**, >2000 vaccinated in responses

*Among participants without elevated levels at entry. P-values between each active vaccine and placebo are significant at level p<0.001 at each visit, except at week 1 for ChAd3 vs. placebo (p=0.004).*

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*Slide courtesy of Rick Davey, NIAID*
Another vaccination strategy
Adenovirus 26 and modified vaccinia virus Ankara–vectored Ebola vaccines

What’s next?

- Studies of durability of protection
- Considerations for use in, eg, pregnant women, children, HIV-infected persons
- Will Ebola vaccine(s) be licensed? And when?
- Multivalent vaccines covering more than Ebola Zaire?
- Consideration of vaccine use strategies
Summary

- Ebola vaccine trials implemented very quickly
- Promising results
  - Single dose rVSV-ZEBOV
  - Other vaccines and strategies
- Stay tuned for more news on licensure, recommendations and guidelines, use strategies

Thank You

The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.