What's coming in adult vaccines and vaccinations?

Ebola vaccine update

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

National Adult and Influenza Immunization Summit
May 10, 2017

Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

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

Photo acknowledgement: WHO Liberia/Peter Glee

Prologue to Ebola vaccine trials

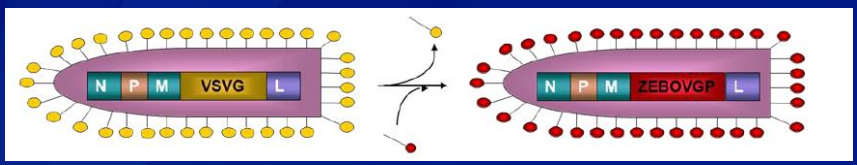
- September 2014: WHO consultation on potential Ebola therapies and vaccines
- Participants concluded there was urgent need to
  - "accelerate [vaccine] development and safe use in countries with outbreaks"
  - " [mount] a coordinated effort by the international community to remove unnecessary obstacles"
- 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)

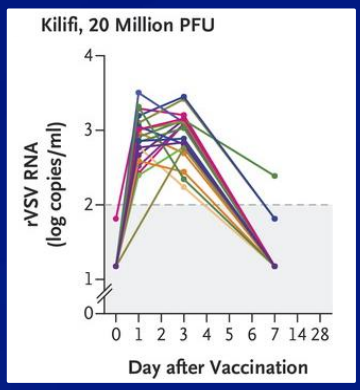


wild type VSV r-VSV-ZEBOV-GP

- Good preclinical record
- Single dose, $2x10^7$ pfu
- Storage at ≤-60°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



Kilifi, Kenya, n=20

Regules JA. N Engl J Med 2015
Agnandji ST et al. N Engl J Med 2016; 374:1647-1660
Huttner A, et al., Lancet Infect Dis 2015; 15:1156-66
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
- 1º outcome laboratory-confirmed Ebola ≥10 days after randomization

Henao-Restrepo AM et al. Lancet. 2015
Henao-Restrepo AM et al. Lancet. 2016

Vaccine efficacy
Ebola ça Suffit trial

	All vaccinated in immediate (group A) vs all eligible and consented on day 0 visit in delayed (group B)	All vaccinated in immediate (group A) vs all eligible in delayed (group B)
Group A		
Number of individuals (clusters)	2108 (51)	2108 (51)
Cases of Ebola virus disease (clusters affected)	0 (0)	0 (0)
Attack rate	0%	0%
Group B		
Number of individuals (clusters)	1429 (46)	3075 (47)
Cases of Ebola virus disease (clusters affected)	10 (4)	16 (7)
Attack rate	0·7%	0·52%
Vaccine effect		
Vaccine efficacy/ effectiveness‡ (%, 95% CI)	100% (63·5 to 100·0)	100% (68·9 to 100·0)
p value§	0·0471	0·0045

Henao-Restrepo AM et al. Lancet. 2016

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

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

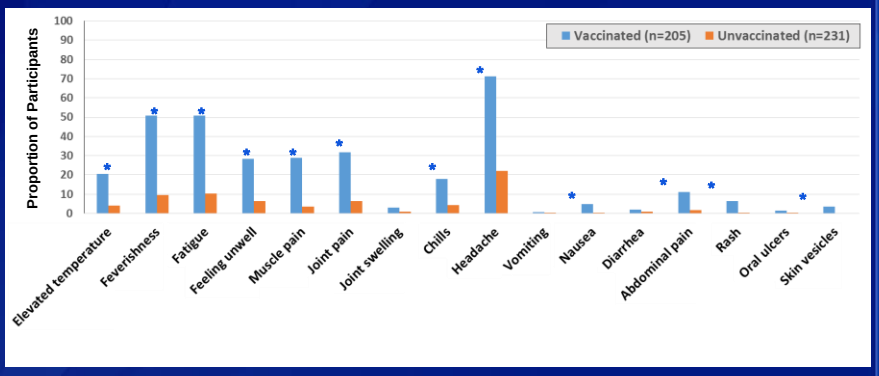
STRIVE high-level results[1]

- **Enrollment and vaccination**
  - Enrolled 8,673 participants (April 9 - August 21, 2015)
  - Vaccinated 7,987
- **Safety profile**
  - Safety/reactogenicity profile consistent with published studies[2]
  - 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

[1]Data are preliminary and results subject to change
[2] Agnandji ST. NEJM 2015; Regules JA.. NEJM 2015; Huttner A. Lancet 2015; Henao-Restrepo AM Lancet 2016; Regules NEJM 2017

STRIVE safety/reactogenicity: 0-7 days

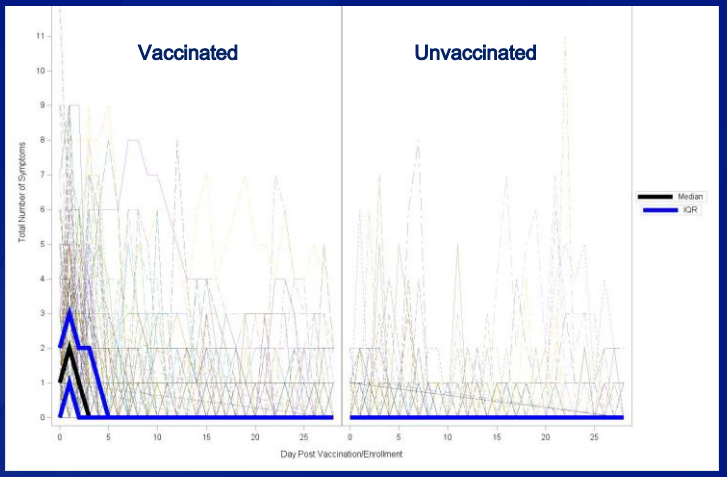
% of participants with solicited adverse events[1]



[1]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 participant[1]



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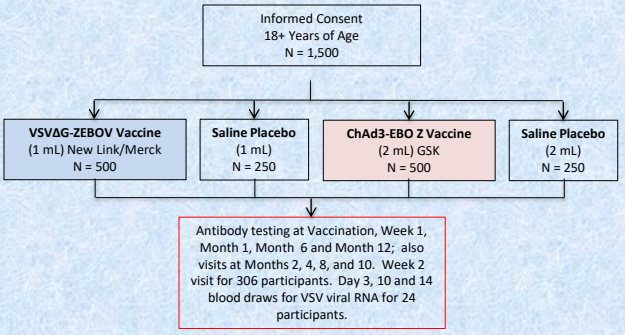
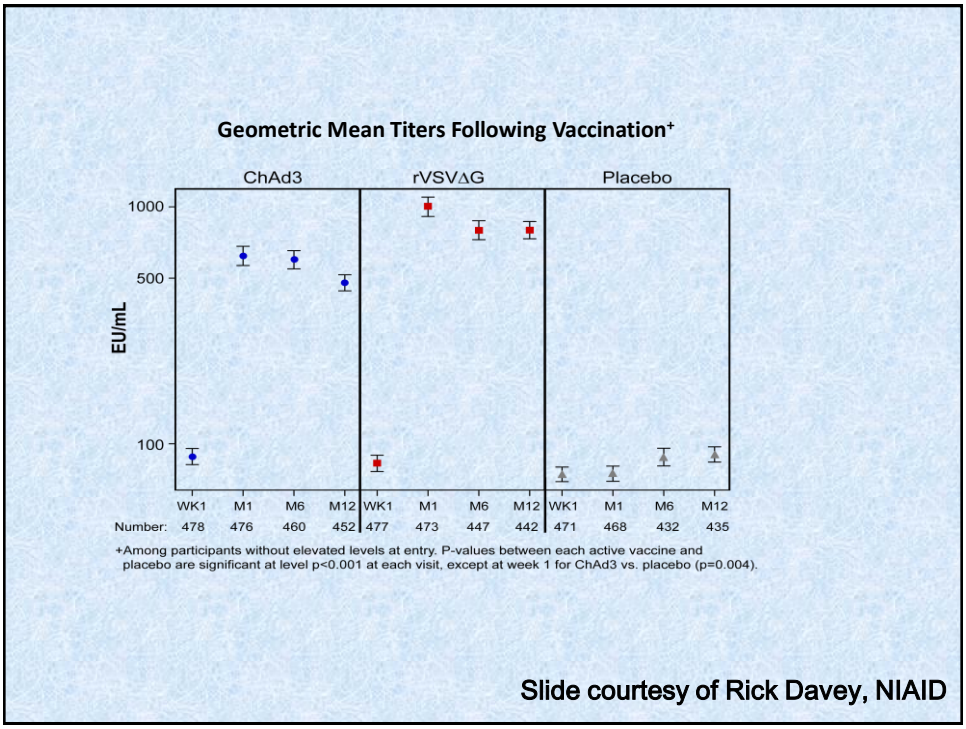
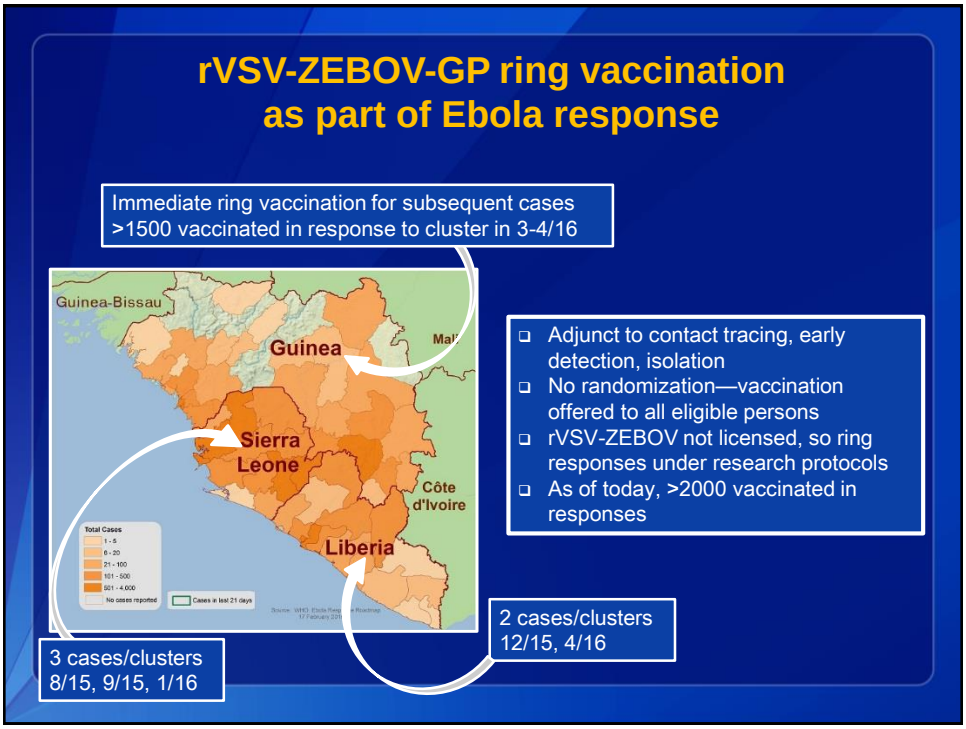
PREVAIL I: Final Protocol



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.

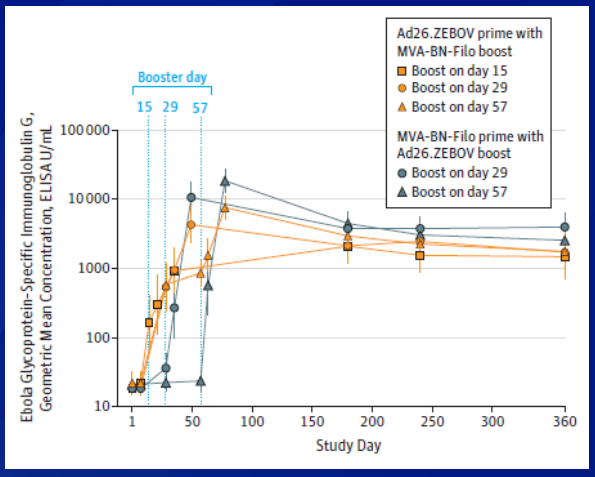
Slide courtesy of Rick Davey, NIAID


Geometric Mean Titers Following Vaccination+
ChAd3
rVSVΔG
Placebo
EU/mL
1000
500
100
WK1 M1 M6 M12 WK1 M1 M6 M12 WK1 M1 M6 M12
Number: 478 476 460 452 477 473 447 442 471 468 432 435
+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).
Slide courtesy of Rick Davey, NIAID


rVSV-ZEBOV-GP ring vaccination as part of Ebola response
Immediate ring vaccination for subsequent cases >1500 vaccinated in response to cluster in 3-4/16
Guinea-Bissau
Guinea
Sierra Leone
Liberia
Côte d'Ivoire
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
2 cases/clusters 12/15, 4/16
3 cases/clusters 8/15, 9/15, 1/16

Another vaccination strategy

Adenovirus 26 and modified vaccinia virus Ankara–vectored Ebola vaccines

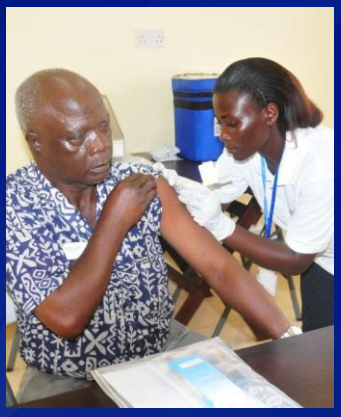


Winslow et al, JAMA 2017

What's next?

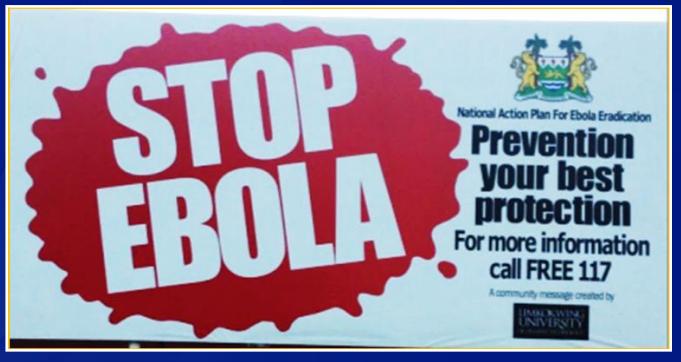
- Studies of durability of protection
- Considerations for use in, eg, pregnant women, children, HIV-infected persons
- Will Ebola vaccine(s) be licensed? And when?
- Multivalent vaccines covering more than Ebola Zaire?
- Consideration of vaccine use strategies

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