Update on Phase 3 Ebola Vaccines Trials
Design and status

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World Health Organization
Phase 3 trials

GUINEA
1. FLW study
2. Ring vaccination RCT
Approx 190 rings.
Immediate vs 21 day.
rVSV vaccine
Started Mar 2015

SIERRA LEONE
Individual RCT
FLWs.
Immediate and deferred
(6 months)
rVSV vaccine
Started April 2015

SIERRA LEONE
Cluster RCT
800,000 vaccine courses.
Randomize by cluster
Ad26/MVA vaccine
Start May 2015.

LIBERIA: "PREVAIL"
Individual RCT
≥27,000 general public.
1:1:1 ChAd3:rVSV:placebo.
Started Jan 2015.

Slide courtesy of Conall Watson
## Ebola vaccines - Phase 3 trials (1)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Location</th>
<th>Doses/ Vaccine(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liberia PREVAIL</td>
<td>Double blinded RCT</td>
<td>Liberia (Redemption Hospital)</td>
<td>ONE DOSE rVSV ChAd3</td>
</tr>
<tr>
<td>Sierra Leone STRIVE</td>
<td>Individually randomized, (unblinded) to immediate or 3 months delayed arm</td>
<td>(Western, Port Loko, Bombali, Tonkolili)</td>
<td>ONE DOSE rVSV</td>
</tr>
<tr>
<td>Sierra Leone MOH/LSHTM/J&amp;JEBOVAC</td>
<td>Cluster randomized (in 3 stages, and 2 arms. Half will be immediate and half delayed by 6 months)</td>
<td>Being finalized (Kambia and potentially other locations)</td>
<td>PRIME + BOOST Ad26 + MVA</td>
</tr>
<tr>
<td>Guinée Ebola ça suffit-essai clinique</td>
<td>Ring vaccination (cluster randomized in areas with EVD) Immediate vs delay (21 days) arms Cohort study among FLWs</td>
<td>Basse-Guinée</td>
<td>ONE DOSE rVSV (ChAd3)</td>
</tr>
</tbody>
</table>
# Ebola vaccines - Phase 3 trials (2)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Sample size</th>
</tr>
</thead>
</table>
| Liberia PREVAIL | Double blinded RCT | Phase 2: 600  
Phase 3: 27,570 |
| Sierra Leone STRIVE | Individually randomized, unblinded | Phase 3: 800  
Safety: 400 |
| Sierra Leone MOH/LSHTM/J&J EBOVAC | Cluster randomised | Stage 1: 40  
Stage 2: 400  
Phase 3/Stage 3: 800,000 (Clusters of approx. 5,000 people) |
| Guinée Ebola ça suffit-essai clinique | Ring vaccination (cluster randomized in areas with EVD) Immediate vs delay (21 days) arms  
Cohort study | 190 rings  
Approximately 10,000 people  
FLWs approx. 1,500 |
Sierra Leone – Phase 3 STRIVE trial

Locations: Western Area, Port Loko, Bombali, Tonkolili
Target: 8,000 Front Line Workers
Sierra Leone
MOH/LSHTM/J&J/
Bavarian Nordic/Crucell
EBOVAC
Geographical distribution of new and total confirmed Ebola cases

Guinée

Ebola ça suffit-essai clinique

Liberia
PREVAIL
## Ebola vaccines - Phase 3 trials (3)

<table>
<thead>
<tr>
<th>Study</th>
<th>Target population</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
</table>
| Liberia PREVAIL              | Individuals at risk for EVD                            | > 18 years         | Fever (38.0 Celsius)  
History of EVD  
Pregnancy (negative urine pregnancy test required) |
| Sierra Leone STRIVE          | Health Workers                                         | > 18 years         | History of EVD or HIV  
Fever (algorithm for evaluation)  
Pregnancy |
| Sierra Leone MOH/LSHTM/J&J EBOVAC | General population                                    | Stage 1:  
18+  
Stage 2 & 3: >12months | Pregnancy, individuals, medically unfit for vaccination through chronic illness |
| Guinée Ebola ça suffit-essai clinique | Eligible individuals who are contacts and contacts of contacts of lab confirmed EVD cases | > 18 years         | Fever  
Pregnancy  
History of EVD or HIV  
History of immunosuppression  
Disease requiring hospitalization at the time of vaccination |
## Ebola vaccines- Phase 3 trials (4)

<table>
<thead>
<tr>
<th>Study</th>
<th>Primary end points</th>
<th>Follow up period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liberia PREVAIL</td>
<td>Ebola Virus Disease (EVD) lab confirmed</td>
<td>Monthly follow-up through event driven closing date</td>
</tr>
<tr>
<td>Sierra Leone STRIVE</td>
<td>EVD lab confirmed</td>
<td>One year</td>
</tr>
</tbody>
</table>
| Sierra Leone MOH/LSHTM/J&J EBOVAC |EVD lab confirmed                             |Stage 1 & Stage 2: 1 year  
Stage 3: 5 months, with 1 year in sentinel groups|
| Guinée Arrêté Ebola    |EVD lab confirmed                             |84 days after vaccination                               |
## Ebola vaccines - Phase 3 trials (5)

<table>
<thead>
<tr>
<th>Study</th>
<th>Number enrolled to date</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liberia PREVAIL</td>
<td>Phase 2: Enrollment completed Phase 3: not initiated</td>
<td>Analysis ongoing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Searching new location</td>
</tr>
<tr>
<td>Sierra Leone STRIVE</td>
<td>Approx. 15 then 40 people/day vaccinated/site. (Unofficial estimate that approx. 100</td>
<td>(Western Rural started last Thursday and Western Urban</td>
</tr>
<tr>
<td></td>
<td>should receive vaccine to date)</td>
<td>started on Monday)</td>
</tr>
<tr>
<td>Sierra Leone MOH/LSHTM/J&amp;J</td>
<td>To start in May 2015</td>
<td>Not recruiting yet</td>
</tr>
<tr>
<td>EBOVAC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guinée Arrêté Ebola</td>
<td>Initiated ring vaccination on March 23, 2015: 8 rings (329 volunteers)</td>
<td>9 teams in the field: 30-40 rings per week</td>
</tr>
<tr>
<td></td>
<td>Initiated FLWs on March 7 FLWS: 222 volunteers</td>
<td></td>
</tr>
</tbody>
</table>
Ebola vaccine trials begin on volunteers in Liberia

Two experimental vaccines are being tested on 600 volunteers in the first phase of trials that authorities hope will eventually include 27,000 people

Associated Press in Monrovia
Monday 2 February 2015 13.38 GMT

A large-scale human trial of two potential Ebola vaccines has started in Liberia’s capital, part of a global effort to prevent a repeat of the epidemic that has now claimed nearly 9,000 lives in west Africa.

The trials in Liberia are taking place after smaller studies determined that the vaccines were safe for human use. By comparing them now with a placebo shot, scientists hope to learn whether they can prevent people from contracting the deadly virus that has killed 60% of those admitted to hospital with the disease.
Guinea Ebola Vaccine Trial Uses Smallpox Strategy

A new Ebola vaccine trial starts in Guinea this week, this one using the same "ring vaccination" strategy that eradicated smallpox in the 1970s.

Ebola vaccines are being tested in all three West African countries hit by the epidemic that's infected 24,000 people and killed 10,000 of them. Two different vaccines are being tested: one that uses an animal virus called vesicular stomatitis virus or VSV, and another using a chimpanzee cold virus called adenovirus.

Both vaccines carry a little piece of the Ebola virus into the body to jump-start an immune response.

"We have worked hard to reach this point," said World Health Organization Director-General Dr. Margaret Chan. "If a vaccine is found effective, it will be the first preventive tool against Ebola in history."

WHO, the Health Ministry of Guinea, Médecins Sans Frontières (MSF, or Doctors Without Borders), and Norwegian Institute of Public Health will start vaccinating volunteers March 7.
Sierra Leone: Ebola Trial Begins

By SHERI FINK    APRIL 13, 2015

Researchers began vaccinating volunteers in Sierra Leone with an experimental Ebola vaccine in a study officially begun on Monday. The trial, the third to begin in the West African countries hardest hit by Ebola, is sponsored by the Centers for Disease Control and Prevention, Sierra Leone’s Health Ministry and the University of Sierra Leone’s College of Medicine and Allied Health Sciences. Scientists aim to enroll 6,000 health workers. The vaccine, rVSV-EBOV, licensed by Merck and NewLink Genetics, has also undergone testing in Liberia, Guinea, the United States and other countries. Earlier research showed that the vaccine is protective in nonhuman primates, but it has not yet been proved to prevent Ebola in humans. The epidemic is declining in Sierra Leone, which on Monday reported two new cases.

A version of this brief appears in print on April 14, 2015, on page A8 of the New York edition with the headline: Africa; Sierra Leone: Ebola Trial Begins.
## Ebola vaccines - Phase 3 trials (6)

<table>
<thead>
<tr>
<th>Study</th>
<th>Partners</th>
<th>Vaccine developers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liberia PREVAIL</td>
<td>MOH Liberia, NIH-USA</td>
<td>GSK</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Merck</td>
</tr>
<tr>
<td>Sierra Leone STRIVE</td>
<td>MOH Sierra Leone, CDC</td>
<td>Merck</td>
</tr>
<tr>
<td>Sierra Leone MOH/LSHTM/J&amp;J</td>
<td>MOH Sierra Leone, LSHTM</td>
<td>J&amp;J</td>
</tr>
<tr>
<td>EBOVAC</td>
<td></td>
<td>Bavarian Nordic, Crucell</td>
</tr>
<tr>
<td>Guinée Arrêté Ebola</td>
<td>Designed by an international effort under the Guinea Working Group.</td>
<td>Merck (GSK)</td>
</tr>
<tr>
<td></td>
<td>Implemented by the Ministry of Health of Guinea, MSF, EPICENTRE and WHO.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Funded by MSF; the Norwegian Research Council through Norway’s Institute of Public Health ; Public Health Agency of Canada, Canadian Institutes of Health Research, International Development Research Center and Department of Foreign Affairs, Trade and Development; and WHO, with support from the Wellcome Trust, UK; sponsored by WHO</td>
<td></td>
</tr>
</tbody>
</table>
Smallpox eradication in West and Central Africa

WILLIAM H. FOEGE,1 J. D. MILLAR,2 & D. A. HENDERSON 3

BULL. WORLD HEALTH ORGAN., Vol. 52, 1975

Smallpox    Ebola

Serial    17 days    15 to 19 days
interval

\( R_0 \)    5 to 7    1 to 2

Vaccine    Effective    Unknown
Works soon    after    Unknown
administration

Fig. 7. Ogoja outbreak, 18-24 December.
What is a vaccination ring?

A vaccination ring is not necessarily a single geographical site. It comprises of:

- all the contacts of an index case of EVD, plus
- household members of any high-risk contact who do not live in the same locality as the case.
- the neighbours or extended family members to nearest geographic boundary in which the local contacts of the index case reside, plus
Example of Chain of Transmission in Guinea

Travel to Guinea Forestiere (Gueckedou, Kissidougou, Macenta) and returned with symptoms

LC, 85 years, Male
Alert: Body is deposited at Donka ETU
Date of Death: 07-11-2014

MT, ? years, Male
Friend of LBC
Community death in Dubreka

MS, 50 years, Female
Mother in law of MT
Admission ETU Donka: 5-12-2014
Date of Death: 24-12-2014
Residence: Gbessia, Conakry

MS, ?, years, Male
Infected his Co Wife whom died in Dubreka.
Date of Death: ?

MS, 48 years, Female
Co Wife of MS
Admission ETU Donka: 24-12-2014
Date of Death: 30-12-2014
Residence: Gbessia, Conakry

MHB, 58 years, Female
Wife of FC
Neighbor of LC
Death in community non secured
Date of Death: 20-12-2014
Residence: Matoto, Conakry

FC, 75 years, Male
Husband of MHB
Neighbor of LC
Death in community non secured
Date of Death: 20-12-2014
Residence: Matoto, Conakry

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Friend of LBC
Community death in Dubreka

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Mother in law of MT
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Date of Death: 30-12-2014
Residence: Gbessia, Conakry

34 Contacts in Matoto, Conakry.
All family members

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All family members

34 Contacts in Matoto, Conakry.
All family members

34 Contacts in Matoto, Conakry.
All family members

27 contacts

19 Contacts in Gbessia and Matoto, Conakry.
All family members

5 Contacts in Matoto + other contacts in Dubreka

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27 contacts
Ring vaccination trial

Newly lab confirmed case of EVD

Definition of ring (Known contacts, contacts of contacts) informed consent and randomization

Random allocation of ring

Immediate vaccination

Follow up for outcomes

Delayed vaccination

Follow up for outcomes

Comparisons

Efficacy

Effectiveness

Eligible, vaccinated
Eligible, not vaccinated
Not eligible, not vaccinated
Community sensitization and informed consent

1. Training of local social mobilizers

2. Initial visit to ring to explain study

3. Collective explanation of ICF

4. Individual ICF with witness
Enrolment and vaccination

1. Eligibility assessment

2. Vaccination

3. 30 minutes observation

4. Individual card and info on next visit
in since the start of the outbreak. There were no confirmed cases maintained throughout the country. In the week to 24 April, the proportion of cases that arose among registered contacts fell slightly, compared with 21 the previous week. Of these data indicate that challenges remain.

In Sierra Leone, coming weeks though surveillance is improving, unknown chains of transmission could be a source of new infections. Each country will retain a core capacity of high-quality Ebola treatment centres, strategically located to ensure complete geographic coverage, with additional rapid-response capacity held in reserve.

A total of 25 confirmed cases of Ebola virus disease (EVD) were reported for the week to 29 March, the most recent week for which data are available. This is the lowest weekly total since the week of May 2014, and the second consecutive week to 56% in the week to 29 March. However, the proportion of cases that arose among registered contacts fell for the week to 22 April, compared with 9 in the previous week.

In the context of falling case incidence and a receding zone of transmission, treatment capacity exceeds demand in Liberia and Sierra Leone. Accordingly, and with technical guidance from WHO, national authorities could be a source of new infections. Each country will retain a core capacity of high-quality Ebola treatment centres, strategically located to ensure complete geographic coverage, with additional rapid-response capacity held in reserve.

A total of 10 prefectures/districts in Guinea and Sierra Leone reported a confirmed case in the week to 5 April, compared with 12 the previous week. Of these data indicate that challenges remain.

In Guinea, 53% were identified in both countries have begun to implement plans for the phased safe decommissioning of surplus facilities. The absence of any reported unsafe burials over the same period, compared with 20 the previous week, is the capital, Conakry, and the low proportion of laboratory samples that test negative for EVD.

In total, 10 prefectures/districts in Guinea and Sierra Leone reported a confirmed case in the week to 5 April, compared with 12 the previous week. Of these data indicate that challenges remain.

In the week to 5 April, Sierra Leone reported zero cases on 3 days during the week to 5 April. In Sierra Leone, coming weeks though surveillance is improving, unknown chains of transmission could be a source of new infections. Each country will retain a core capacity of high-quality Ebola treatment centres, strategically located to ensure complete geographic coverage, with additional rapid-response capacity held in reserve.

This is the week to 22 April, compared with 9 in the previous week.

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Many thanks