Using the expanded access/compassionate use to evaluate rVSV-EBOV-GP in DRC

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Filovirus Clinical Research Workshop, 20-22 février, Uganda, 2024
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Ebola virus disease in the DRC

Ebola Virus disease

- Ebola virus disease (EVD), formerly known as Ebola hemorrhagic fever, is a severe, often fatal illness affecting humans and other primates.

- Since the discovery of the Ebola virus (1976), the DRC has experienced the highest number of Ebola Virus Disease (EVD) epidemics on record.

- The DRC reports 15 outbreaks of the Ebola virus, the last 6 epidemics have occurred in the last 6 years.

- In terms of loss, we are among those (countries) who have lost many people to this disease.
**First use of rVSV-EBOV-GP vaccine**

**Clinical Research Protocol**

- In 2017, a research protocol for a clinical trial using rVSV-EBOV-GP vaccine was developed and has been formally approved by the DRC national authorities and the Ethics Committee.

- For the first time, the Congolese government has authorized the vaccination of all health personnel going to work in **Likati** in 2017.

- In the affected area, there was a vaccination campaign, we vaccinated people targeting "primarily **healthcare personnel, contacts of the sick** and **contacts of contacts**".

- The introduction of Ebola vaccine in 2017, in particular rVSV-EBOV-GP was a major step forward.
First use of rVSV-EBOV-GP Vaccine (2)

Progress and End of the Ebola outbreak in 2017

• Unfortunately, the clinical trial was short-lived, as the end of the epidemic was declared two months later (Mai - July 2017).
  
  • Summary of the Outbreak:
    ✓ 4 deaths out of 8 confirmed cases
    ✓ ≈ 600 suspected cases have been vaccinated

Lessons learned from 2017 vaccination:

• This first vaccination against Ebola disease (in 2017) gave us initial feedback from the community.
  • **Acceptability**: Majority of people accepted given the lethality rates
  • **Side effects**: many side effects were observed including vomiting, fatigue, Soreness, Headache, chill at night etc...
  • **Some people refuse to be vaccinated**: because the side effects were enormous
  • **Contamination**: less
Large-scale use of rVSV-EBOV-GP vaccine

Ebola disease outbreak in 2018
- The 10th Ebola outbreak in DRC (longest and largest).
  - Longest: 2 years (2018-2020)
  - Largest: Affected 3 provinces in the eastern part of DRC
    - Number of positive cases: 3,470 cases
    - Deaths: 2,287 cases (≈ 65%)

- During this epidemic, the use of Ebola molecules and vaccines was tested on a large scale.
  - Drugs: ZMAP, MAB114, REMDESIR…
  - Vaccines:
    1. rVSV-EBOV-GP vaccine
    2. JnJ vaccine (clinical Trial)
Large-scale use of rVSV-EBOV-GP vaccine (2)

Context of the 10th Ebola outbreak Outbreak

- The epicenter of the 10th Ebola outbreak was in Beni and Butembo located in the north Kivu of province, then spread to Ituri and Sud Kivu Provinces.

- The epidemic was difficult to manage for several reasons:
  1. it was difficult to reach all the affected areas because they were under the control of rebels or armed groups.
  2. there were many rumors about the disease, and the community had little knowledge of it.
  3. Most of the staff working on the response were not from the community (they came from elsewhere).

- All of the above factors did not allow proper management of the disease, leading to contamination and an increase in the number of deaths in the country.
Ebola outbreak Management

- After several internal meetings, we realized that for a good management of the outbreak will need to integrate certain measures in particular:
  - To increase community involvement activities (radio messages, ...)
  - To raise awareness by involving community leaders
  - To use local manpower (nurses and doctors).
  - To work also with the security services for the protection of the staff.

- The same protocol approved for the 9th epidemic was renewed with a change of province since the 10th epidemic was in North Kivu.

- In total 37 health zones were affected, and the field team struggled to follow up on suspected cases and vaccinate as much possible all eligible cases.
# Large-scale use of rVSV-EBOV-GP vaccine (4)

## Number of vaccinated by category

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of vaccinated</th>
<th>Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child</td>
<td>1,598.00</td>
<td>2018-2020</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>1,310.00</td>
<td>2018-2020</td>
</tr>
<tr>
<td>Breast-feeding women</td>
<td>5,559.00</td>
<td>2018-2020</td>
</tr>
<tr>
<td>Adults</td>
<td>295,438.00</td>
<td>2018-2020</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>303,905.00</strong></td>
<td><strong>2018-2020</strong></td>
</tr>
</tbody>
</table>
## Assessment factors

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Intervention</td>
<td>Clinical trial</td>
<td>Clinical trial/Prequalified 2019</td>
</tr>
<tr>
<td>Vaccination Strategy</td>
<td>Ring Vaccination</td>
<td>Ring Vaccination</td>
</tr>
<tr>
<td>Administered dose</td>
<td>1 vial for 10 participants</td>
<td>1 vial for 20 participants (reduced doses)</td>
</tr>
<tr>
<td>Number of vaccinated</td>
<td>600</td>
<td>303,905.00 (women, child, adult)</td>
</tr>
<tr>
<td>Side effects</td>
<td>Many</td>
<td>Less</td>
</tr>
<tr>
<td>Level of immunity</td>
<td>Conferred good protection</td>
<td>Conferred good protection</td>
</tr>
</tbody>
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Prequalification steps for rVSV-EBOV-GP

**2016**
- **JULY 25**
  - US FDA granted vaccine Breakthrough Therapy Designation, and EMA granted PRIME (PRIority MEDicines) status

**2018**
- **NOVEMBER 13**
  - Submission of a rolling Biologics License Application to the US FDA

**2019**
- **FEBRUARY-JULY**
  - In collaboration with FDA and EMA, submission made to WHO to achieve prequalification status and to African health authorities in collaboration with the AVAREF
- **MARCH 11**
  - EMA accepted Marketing Authorization Application for review
- **SEPTEMBER 17**
  - US FDA accepted Biologics License Application and granted priority review
- **OCTOBER 18**
  - EMA CHMP gave positive opinion recommending conditional marketing authorization
- **NOVEMBER 11**
  - Granted conditional marketing authorization in the EU
- **NOVEMBER 12**
  - WHO prequalification
- **DECEMBER 19**
  - Approved by US FDA for prevention of disease caused by Zaire ebolavirus in individuals aged ≥18 years

**2020**
- **FEBRUARY 14**
  - Approved in five African countries (Burundi, Democratic Republic of the Congo, Ghana, Guinea, and Zambia) within 90 days of reference country approval and WHO prequalification
Benefits of rVSV-EBOV-GP vaccination

• All data collected by previous vaccinations (Guiné 2016, Likati 2017, Bikoro 2018) have enabled the rVSV-EBOV- GP vaccine to be prequalified in 2019 by the WHO.

• Interesting and easy to use during the epidemic with a single dose of vaccination. Given that two-dose vaccines are often difficult to use during epidemics.

• According to data collected, the risk of death was 56% for unvaccinated patients but dropped to 25% for those who had received the vaccine. This reduction in mortality applied to all patients, regardless of age or gender.

• In addition to the direct benefit, some results showed the risk of illness and death for patients who have been in direct contact with a positive case of Ebola has been reduced when they got the combination of vaccine and drug against Ebola.
**Conclusion**

**Booster vaccination**

- Booster vaccination with rVSV-EBOV-GP vaccine is important because the duration of Ebola antibodies in the body is not clearly defined (immunogenicity study).

  - **In DRC**: Ebola outbreaks are now more frequent

- Booster vaccination to prevent re-emergence of the virus from the sperm and mother’s milk
THANK YOU

STOP EBOLA