Experience integrating therapeutics trials as part of outbreak response

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Building research readiness for a future Filovirus outbreak Feb 20-22 2024, Uganda
Outline of the presentation

I. EVD response & care from MEURI to RCT

II. Lessons learned
I. EVD response & Care from MEURI to RCT
May 8, 2018
Outbreak declared
2 samples from Bikoro confirmed Ebolavirus +

May 17, 2018
4 cases confirmed in Mbandaka

May 21, 2018
WHO raises Ebola health risk to 'very high'

May 29, 2018
DRC IRB approved Remdesivir and Favi

May 18, 2018
WHO and MoH start rVSV vaccination in Mbandaka

June 1, 2018
DRC IRB approved Zmapp, REG-3EB and Mab114

June 6, 2018
Last confirmed case

Jul 24, 2018

Aug 1st, 2018
Outbreak declared

Aug 6, 2018
INRB sequencing confirmed Zaire Ebolavirus supporting the use of rVSV, Zmapp & Mab114

Aug 7, 2018
IRB approved EAP for rVSV-EBOV & mAb114

Aug 8, 2018
Arrival of INRB clinicians in Beni

Aug 10, 2018
WHO & MoH start rVSV “ring” vaccination in Mangina

INRB treats 2 Ebola patients under EAP in Mangina Hospital

Aug 11-13, 8 more patients treated in Mangina Hospital

Aug 15, 2018
Establishes a 74 beds ETU in Mangina

Aug 17, 2018
IRB approved EAP for Zmapp, Remd, REGN-3 EB

Aug 20, 2018
ALIMA establishes 16 beds ETU with 5 Cubes in Beni
EVD in eastern DRC & the MEURI

Arrival of INRB clinicians in Beni, 7 Aug 2018

First 2 cases cured from Ebola after receiving mAb114 in Mangina
• Hourly clinical monitoring (vital sign and symptoms)
• Follow up blood chemistry (Crea, AST/ALA, Na, Glu..)
• Provide optimized standard of cares
• Monitoring of CtNP value (viral load)

Clinical, chemistry and virology parameters suggested that IP did not harm the patients. All treated patients survived (CFR=0%). The overall CFR during the outbreak was 67%
First time Ebola vaccine & therapeutics are available at early phases of the outbreak (prepositioned in the field & at INRB Kinshasa).

Preparatory steps: 1) Expanded Access Protocol (EAP) writing, 2) Training of staff, 3) IRB review & Logistic for MEURI (Vaccine & Treatment) → 3-4 weeks

Shorter timing for implementation of the EAP (vaccine/therapeutics) in North Kivu (< 10 days) versus Equateur

EAP provided an ethical framework to give access to IP & optimized standard care for a large number of EVD patients during emergency situation

EAP paved the way for the RCT protocol to determine the efficacy of IP
Sponsor: NIAID DCR, **Oversight and execution**: INRB

**Objective:** To study the safety and effectiveness of 4 drugs for people with Ebola virus

**Study Process:**
- ZMapp: ~ 4 hours. (3 days interval)
- Remdesivir: ~ 1 hour. (10 days, 1x/day)
- mAb114: 30-60 minutes
- REGN-EB3: ~ 2 hours.

**PRODUITS EXPERIMENTAUX UTILISÉS DANS LE RCT**

<table>
<thead>
<tr>
<th>Category</th>
<th>Cocktail d'anticorps monoclonaux chimériques humains-murins</th>
<th>combination of three human monoclonal antibodies</th>
<th>Unique Anticorps monoclonal humain</th>
<th>Nucleotide prodrug</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZMAPP</td>
<td>Zaire Ebolavirus</td>
<td>Zaire Ebolavirus</td>
<td>Zaire Ebolavirus</td>
<td>antiviral a large spectre</td>
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<tr>
<td>REGN-3B</td>
<td>Single Dose</td>
<td>Single Dose</td>
<td>10-14 Day course</td>
<td></td>
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<tr>
<td>Mab-114</td>
<td>3 Doses – Day 0, 4, 7</td>
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Cumulative incidence of death in the overall population

mAb114 and REGN-EB3 reduced significantly the mortality from EVD compared to Zmapp
Care from DRC EVD 10 and onwards

- Isolation
- Administration of therapeutics
  + Standard of Care + Clinical follow-up
- Discharge

Lab confirmation (Diagnostic)
- Assessing efficiency of therapeutics:
  - Follow-up of patients treated
  - (Blood chemistry, hematology, virology)
- Discharge
Ebola virus Reservoir
- Ecological studies
- Circulation of the virus in the reservoir
- Dynamic of the virus in the environment
- Interaction at human/animal interface

Confirmed-cases
- Role of therapeutics on the immunity
- Diagnostic tools: serology
- Interaction at human/animal interface

Ebola survivors
- Biological, immunological & virological follow-up...
- Immune privileged sites & relapses
- Pregnancy & Immunodepression

Economical & Logistics
- Availability of therapeutics in LMICs
- Poor resources
- Logistics: transportation, storage & distribution (cold chain)
II. Lessons learned
Field performance of three Ebola rapid diagnostic tests used during the 2018–20 outbreak in the eastern Democratic Republic of the Congo: a retrospective, multicentre observational study

Conducting research capabilities in the field during EVD outbreaks...

Head-to-head comparison of diagnostic accuracy of four Ebola virus disease rapid diagnostic tests versus GenExpert® in eastern Democratic Republic of the Congo outbreaks: a prospective observational study

Virus kinetics and biochemical degradations among children with Ebola virus disease

Integration of genomic sequencing into the response to the Ebola virus outbreak in Nord Kivu, Democratic Republic of the Congo
Building new research capacities...INRB Kinshasa
Building new research capacities: INRB Goma & Beni

2019...
- Lyon, October 2019
- Goma, October 2019
- Goma, November 2019
- Goma, June 2020
- Goma, July 2020
- Goma, June 2020

Today...
- INRB-Goma
  - BSL-3 Lab
  - BSL-2 Lab
  - Genomics
  - Clinical-Biology Lab
  - Bacteriology
  - Immuno-Serology Lab
  - Molecular biology

- INRB Beni
  - Functional cold chain
  - Power Supply
  - Administrative building
  - Mobile BSL-2
  - Mobile Lab-outreach
Use of point-of-care: Diagnostic & follow-up…

1. Blood chemistry, hematology & gas

2. Molecular assays
Biorepository in Kinshasa & Goma for Ebola positive samples...

Approx 400,000 Samples stored in the Biorepository
- Ebola (9th to 14th outbreaks) : samples (plasma and oral swabs) — negative and positive
- Mpox : samples (plasma, vesicles and scabs) — negative and positive
- Wildlife (bats and rodents) : Oral and rectal swabs, and tissues
- Measles : oro-pharyngeal swabs
- Covid-19 : oro-pharyngeal swabs
- PALM001 (Ebola RCT) samples : plasma
- PALM006-inVITE (observational study on Covid-19) samples
- PALM007 (Mpox RCT) samples : blood, swabs and skin lesions

~ 500,000 samples: Ebola, Plague, mpox, Cholera, SARS-CoV-2, Antrax, meningitis, Measles...
Local workforce = capacity building → Empowerment/Dx decentralization

1) Clinical trials, 2) Data handling & management, 3) Ethics & RGPD, 4) IATA, biosafety, biosecurity, 5) Operation of high containment infrastructures (ETU, Laboratories), 6) patients recruitment strategies, 7) instruments manipulation/troubleshooting, 8) sequencing capacity…
Organizational chart for field laboratories used for Ebola virus disease outbreak during chronic insecurity, eastern Democratic Republic of the Congo, 2018–2020. INRB, Institut National de Recherche Biomédicale.
Aksanti
Merci
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