Process for prioritization and current recommendations for the evaluation of candidate therapeutics

United in Solidarity against Filovirus threats

Kampala, Uganda, 20-22 February 2024

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EMA
Only a handful of platform trials were informative

As of Aug 02, 2023 there were 4634 randomized trials of COVID-19 treatments

Most trials were not informative and some were too small to be able to answer confidently key public health questions.

Some of the treatments evaluated maybe should have not been prioritised

Improvements are needed in the South and in the North!
Regarding access to candidate therapeutics during outbreaks and pandemics, some have emphasized the importance of **speed** and sometimes **cost** in responding to future pandemics.

It is equally important to take a broader view that recognizes the primary importance of **quality**, **equity** in availability, and **trust** in the products safety and efficacy.
Being prepared to integrate research during outbreaks

Data-driven decisions by **open collaborative scientific networks**

**MOH in the driving seat**
- Designates researchers
- Support of local research capacity
  - Local researches contribute to the process

**Landscapes of candidates**
- Target Product Profiles
- Independent process for prioritization
  - A virtual process to ensure **therapeutics are available** for outbreak evaluation

**Pre-outbreak trial design**
- Pre-approved CORE protocol
- Legal, regulatory and insurance framework
  - Support of local research capacity

**Research and innovation priorities for other areas**
Inter-epidemic research for Filovirus family

An example, leading toward a Viral family approach
Outbreaks research for Filovirus family

An example, leading toward a Viral family approach
A WHO Global Committee for prioritization of candidate treatments for evaluation during outbreaks

Established in early 2020
Independent experts, transparent, data-driven, with a priori defined criteria

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Number of products reviewed</th>
<th>Type of product</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19</td>
<td>Over 20</td>
<td>• Antiviral&lt;br&gt;• Inmunomodulators&lt;br&gt;• Antimalarials</td>
</tr>
<tr>
<td>Sudan ebola virus</td>
<td>7</td>
<td>• MAbs cocktail and MAb&lt;br&gt;• Antiviral&lt;br&gt;• Therapeutic to target host response</td>
</tr>
<tr>
<td>Marburg</td>
<td>3</td>
<td>• MAbs cocktail and MAb&lt;br&gt;• Antiviral</td>
</tr>
</tbody>
</table>
An existing open collaborative scientific network (MARVAC) was triggered immediately after Sudan ebolavirus outbreak declaration.

8 consultations on candidate treatments were held between Aug-Nov 2022.

Approx 50 scientists per meeting (and 500+ for global consultations)

- clinicians/researchers from the Uganda MOH, ETCs,
- filovirus experts, clinical trial experts, developers

Topics discussed included:

1. Evidence regarding different investigational therapeutic agents
2. Study design and opportunities for implementation of a clinical trial.
3. Proposed CORE protocol based on the prioritized trial design options.

*Prioritization of Treatment Study Designs*

<table>
<thead>
<tr>
<th>Option</th>
<th>Trial Design Option</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Standard of care (SOC) + Monoclonal versus SOC + Antiviral versus SOC + Monoclonal + Antiviral versus SOC alone (Full factorial) design. Secondary randomization corticosteroids</td>
<td>Including a SOC arm will permit the most valid and interpretable estimation of potential treatment effect. This design is efficient and could provide the results relatively quickly.</td>
<td>As the candidate therapeutics are already in use, the SOC arm was considered less acceptable for a disease with very high baseline mortality.</td>
</tr>
<tr>
<td>2</td>
<td>SOC + Monoclonal versus SOC + Monoclonal + Antiviral versus SOC alone Secondary randomization corticosteroids</td>
<td>Including a SOC arm will permit the most valid and interpretable estimation of potential treatments effect. This design will provide understanding on the impact of the monoclonal and the synergistic impact of the combination therapy.</td>
<td>As the candidate therapeutics are already in use, the SOC arm was considered less acceptable for a disease with very high baseline mortality. The design does not provide direct information on the effect of the antiviral alone.</td>
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<tr>
<td>3</td>
<td>SOC alone Secondary randomization corticosteroids</td>
<td>If an SOC alone cannot be implemented, this design can provide evidence on any differential effect of monoclonal antibodies vs antiviral, and on any efficacy of the two.</td>
<td>If the synergic effect of a monoclonal plus an antiviral is low, the sample size could increase.</td>
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</tbody>
</table>
An existing open collaborative scientific network (MARVAC) was triggered immediately after Marburg outbreak declaration.

4 consultations on candidate treatments were held between Feb – Jul 23.

Approx 30-50 participants and 500+ for global consultations.

Items discussed included:
- Review of available vaccines and therapeutics, status, and availability
- Review a CORE trial protocol

With special thanks to Peter Horby, Amanda Rojek, Martin Landray, and colleagues at the Univ of Oxford for developing the full protocol based on the outputs of the global consultations.
Being prepared to integrate research during outbreaks

- Refine the procedures around product prioritisation and clinical trial design with selected panel of independent experts

- Continue to foster collaboration for evaluating candidate therapeutics within outbreak responses

- Give the opportunity to national researchers and authorities to contribute to design of trial protocols for candidate vaccines and therapeutics towards final consensus on key trial design attributes.

- Develop an action plan per pathogens for collaborative network of designated researchers in “at risk” countries via engagement in a framework for clinical research preparedness to ensure clinical research is promptly integrated into future outbreak responses.
Maximizing our research efforts to inform strategic actions is critical to control outbreaks and prevent future pandemics.

“A systematic approach that studies treatments against representative pathogens from families with known pandemic potential to be better prepared vs. emerging or reemerging pathogens”.

Innovative approaches and emerging technologies, e.g. Mab platforms, broad-spectrum antivirals or host-therapies, can help select among available candidate treatments for prototype pathogens.
Thank you