Assessing Impact of Access to mRNA Vaccines in LMICs

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An Exploding Ebola Outbreak in mid-2014

Cases reported per week
Week of 2014
Ebola in Guinea, Liberia, Sierra Leone
Liberia
Sierra Leone
Guinea
up to 21 September

March 24  May 19

Chris Dye, WHO
# Ebola Vaccine Trial Timeline

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 August</td>
<td>Grant application submitted</td>
</tr>
<tr>
<td>26 August</td>
<td>Award letter</td>
</tr>
<tr>
<td>30 August</td>
<td>Vaccine filled</td>
</tr>
<tr>
<td>2 September</td>
<td>Trial file submission to UK regulator</td>
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<tr>
<td>5 September</td>
<td>Ethics meeting</td>
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<tr>
<td>8 September</td>
<td>Ethical approval</td>
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<tr>
<td>9 September</td>
<td>Regulatory approval</td>
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<tr>
<td>11 September</td>
<td>Vaccine shipping</td>
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<tr>
<td>15 September</td>
<td>Vaccine labelled</td>
</tr>
<tr>
<td>16 September</td>
<td>Trial contract signed</td>
</tr>
<tr>
<td>17 September</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; vaccinee</td>
</tr>
<tr>
<td>18 November</td>
<td>60&lt;sup&gt;th&lt;/sup&gt; vaccinee</td>
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Declining Case Incidence

Vaccine trials in the outbreak area delayed until April 2015

Only one vaccine was tested: Merck’s VSV-vectored vaccine expressing Ebola glycoprotein

Very high efficacy

Requires ultra-low temperature storage, manufacturing process not scaled-up

J&J vaccine now also licensed

Vaccines cover Ebola Zaire only
<table>
<thead>
<tr>
<th>Virus</th>
<th>Country of first identification</th>
<th>Year of first identification</th>
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<tbody>
<tr>
<td>Crimean Congo haemorrhagic fever (CCHF)</td>
<td>Crimea and Congo</td>
<td>1967</td>
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<tr>
<td>Ebola</td>
<td>South Sudan and Democratic Republic of Congo</td>
<td>1976</td>
</tr>
<tr>
<td>Marburg</td>
<td>Germany and Serbia (from NHPs imported from Uganda)</td>
<td>1976</td>
</tr>
<tr>
<td>Lassa fever</td>
<td>Nigeria</td>
<td>1969</td>
</tr>
<tr>
<td>SARS-CoV-1</td>
<td>China</td>
<td>2003</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>China</td>
<td>2020</td>
</tr>
<tr>
<td>MERS-CoV</td>
<td>Saudi Arabia</td>
<td>2012</td>
</tr>
<tr>
<td>Nipah</td>
<td>Malaysia</td>
<td>1999</td>
</tr>
<tr>
<td>Rift Valley fever (RVF)</td>
<td>Kenya</td>
<td>1931</td>
</tr>
<tr>
<td>Zika</td>
<td>Uganda</td>
<td>1947</td>
</tr>
<tr>
<td>Severe fever with thrombocytopenia syndrome (SFTS)</td>
<td>China</td>
<td>2009</td>
</tr>
<tr>
<td>Chikungunya</td>
<td>Tanzania</td>
<td>1952</td>
</tr>
<tr>
<td>Hendra</td>
<td>Australia</td>
<td>1994</td>
</tr>
</tbody>
</table>
Middle East Respiratory Syndrome coronavirus (MERS-CoV)

• More than 2250 cases of severe acute respiratory disease, 800 deaths in 27 countries
• Camels are the source of zoonotic infections
  – Occupational exposure can lead to seroconversion
  – Severe disease in the immunocompromised
  – Hospital outbreaks
• Major surface antigen is the Spike (S) protein
ChAdOx1 MERS immunogenicity

Folegatti et al., Lancet Inf Dis 2020
From the ChAdOx1 platform to a vaccine candidate against COVID-19

104 days from sequence to humans

- Vaccine design begins
- First batch of GMP vaccine started
- First human trial begins in UK in 1000 volunteers (Phase I/II)
- Late-stage trial begins in Brazil in ~10,000 volunteers (Phase III) and in South Africa in ~2000 volunteers (Phase I/II)
- Late-stage trials ongoing in more than 30,000 volunteers in the USA (Phase III)
- Japan study starts (Phase I/II)
- India study starts (Phase I/II)
- Russia study starts (Phase III)
- Kenya study starts (Phase I/II)
- Authorized for use in India and the EU
- Authorized for emergency supply in the UK
- Authorized for emergency use by WHO
- Pediatric trial announced

WHO declares public health emergency of international concern
Virus genetic sequence available
First cases outside mainland China
First human trial begins in UK in 1000 volunteers (Phase I/II)
Late-stage trial begins in more than 10,000 volunteers in UK (Phase II/III)
Late-stage trial begins in Brazil in ~10,000 volunteers (Phase III) and in South Africa in ~2000 volunteers (Phase I/II)
Late-stage trials ongoing in more than 30,000 volunteers in the USA (Phase III)
Japan study starts (Phase I/II)
India study starts (Phase I/II)
Japan study starts (Phase I/II)
Authorized for emergency supply in the UK
Authorized for emergency use by WHO
Pediatric trial announced

Worldwide cases pass 100 million
Worldwide cases pass 10 million
Worldwide cases pass 5 million
First cases outside mainland China
Virus genetic sequence available

Collaboration has made this possible

EU = European Union; GMP = Good Manufacturing Practices; UK = United Kingdom; USA = United States of America; WHO = World Health Organization.

Equitable access strategy delivers vaccine at no profit to over 170 countries: over 25 manufacturers in 15 countries

- Parallel supply agreements to ensure global access.

- First AZ vaccine doses not yet delivered
- First AZ vaccine doses have been delivered

- Countries eligible to receive AZ vaccine through COVAX

- Continued engagement with int'l orgs and gov'ts to drive equitable access
Supporting equitable access, globally

Key points

• 128 approvals and emergency authorisations in ~100 countries to date
• More than 2.8 billion doses released for supply to 180 countries
• Collaboration with more than 20 partners across over 15 countries
• 424 million doses to approx 130 countries via COVAX
• Approx. 2/3 doses to low and lower middle income countries
Of the first 38 million doses administered via Covax, 37 million doses were ChAdOx1 nCoV-19
Vaccine effectiveness data

• Public Health England data released March 1\textsuperscript{st}.

• In England, in over 70s who have received one dose, from 28 days, at least 60% protection against symptomatic PCR +ve disease (ChAdOx1 nCoV-19 and also BNT162b2)

• In over 80s, hospitalisation reduced by 80% (ChAdOx1 nCoV-19 and also BNT162b2)

• Deaths in over 80s reducing faster than in younger age groups (combined effect of ChAdOx1 nCoV-19 plusBNT162b2)
Why produce mRNA vaccines in LMICs?

In outbreak/epidemic scenarios
- Rapid access
- Rapid deployment
- Ability to control pricing
- Independent planning of vaccine development and stockpiling
  - or plans for rapid production when needed

For routine vaccination programmes
- Control of supply locally
- Ability to control pricing
- Development of sustainable industry
- Advancement of the technology is possible
  - Ambient temperature storage?
  - Mucosal delivery?
What challenges can be expected?

• Intellectual Property
• Regulatory concerns
  • Local regulatory capacity must be strengthened
  • Distributed manufacturing results in a complex situation for regulators
  • Ultra-local manufacturing presents further challenges
• For routine vaccinations, prices may be higher
• Secure supply of raw materials
• For outbreak pathogens,
  • how to prioritise? Local planning.
  • how to plan for efficacy testing? Global planning.
  • how to plan for rapid response? Local and global planning.
• Facilities must be ‘kept warm’
• Should livestock vaccines be produced and rolled out?
PANDEMIC SCIENCES INSTITUTE (PSI)

• The Pandemic Sciences Institute will draw upon lessons learnt from COVID-19 pandemic to identify and counter future pandemic threats
• Partnership between academia, industry & public health organisations across the world
• Create science-led innovations to
  • accelerate the understanding
  • develop new diagnostics, treatments, vaccines & digital control tools
• Focus on equitable access