Current Status of Ebola Vaccines and Treatments

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Disclaimer: The views expressed herein are solely the responsibility of the authors and do not necessarily represent the official views of the CDC.
Treatment and Vaccines for Ebola Virus Infection

- **Current Status of Vaccines**
  - 15 open studies on clinical trials.gov

- **Current Status of Treatments**
  - 8 open studies on clinical trials.gov

- Challenges

- Opportunities
Current Status of Vaccines

- Lead candidates
  - Recombinant VSV (rVSV)
  - Recombinant adenoviruses
- Ongoing studies
  - Classic, placebo controlled RCT (Liberia)
  - Immediate vs. deferred RCT (Sierra Leone)
  - Ring vaccination (Guinea)
Patients who Survive Acute Ebola virus Infection do so with a Disappearance of Circulating Virus and What Appears to be a State of Protective Immunity
Unfortunately, no Clear Correlate of that Protective Immunity has been Established Making Vaccine Development a Significant Challenge and Emphasizes the value of a Clinical Endpoint Study
Most Advanced Investigational Candidate Ebola Virus Vaccines

- Recombinant Vesicular Stomatitis Virus
  - Replication competent
  - Local and systemic reactions in approximately 50%
  - Transient arthralgia in approximately 30% with one site reporting a series of cases of reactive arthritis

- Recombinant Chimpanzee Adenovirus 3
  - Not replication competent
  - Local and systemic reactions in approximately 50%
  - Prolongation of PTT
Prevail Study Design Overview

https://clinicaltrials.gov/ct2/show/NCT02344407

 Individuals at Risk for EVD (HCW, Contact Tracers, Burial Teams, Individuals living in outbreak area etc.)

- **rVSVΔG-ZEBOV Vaccine** (N = 9,000)
- **ChAd3-EBO Z Vaccine** (N = 9,000)
- **Saline** (N = 9,000)

**Labs at Baseline**
- Week 1
- Week 4 (n=600)

**Weekly follow-up x1; then monthly follow-up through event driven closing date**
Associated Press
February 2, 2015

Ebola Vaccines Testing Starts in Liberia

- Phase II/III trial; goal is 27,000 volunteers
- cAd3-EBOZ vs. rVSV-EBOV vs. placebo
Screening Volunteers for Participation in the Prevail Vaccine Study at Redemption Hospital
Additional Vaccine Candidates and Designs

- Immediate vs. deferred step-wedge study of rVSV (Sierra Leone MoH/CDC/WHO) - recruiting  
  https://clinicaltrials.gov/ct2/show/NCT02378753
- Immediate vs. deferred ring vaccination study of rVSV (Guinea; WHO)
- Ad26 prime / MVA boost (Johnson/Johnson + Bavarian Nordic)
- Multiple other platforms including rabies virus and parainfluenza virus
Current Status of Treatment

- Supportive Care
  - Fluid and Electrolyte replacement
  - Ventilator Support
  - Renal Replacement Therapy
- Anti-viral strategies
  - Antibody based therapies
  - Small molecule inhibitors
  - Anti-sense molecules
Therapeutic Targets in the Ebola Life Cycle

Neutralizing Antibodies
- Convalescent serum
- Monoclonals

Nucleos/tide Analogues
- Brincidofovir
- Favipiravir
- BCX 4430

Antibody-dependent Cellular Cytotoxicity
- Convalescent serum
- Monoclonals

Anti-sense mRNA-binding molecules
- Tekmira
- Sarepta

Adapted from White & Schonberg, Nat Rev Micro (2012) 10:317
ZMapp Monoclonal Antibody Candidate Treatment

ZMapp Structure by Electron Microscopy

Ebola Virus Glycoprotein GP

Non-Human Primate Challenge

![Graph showing survival rates]


ZMapp, other mAbs, Convalescent Plasma & Whole Blood

- ZMapp Trial ongoing – no new cases
- Chinese mAb – yet to enter clinical Trials
- Convalescence blood trials underway
- None of these trials likely to provide decisive efficacy data
Due to the Improvements in Supportive Care and Variability in Disease Presentation, Historical Controls Have the Potential to be Misleading.
# Changing Mortality for Ebola Virus Infection Over Time

<table>
<thead>
<tr>
<th>Date</th>
<th>N</th>
<th>Site</th>
<th>Mortality</th>
<th>Change from Prior Interval</th>
<th>Change from May-June</th>
</tr>
</thead>
<tbody>
<tr>
<td>May-June, 2014*</td>
<td>106</td>
<td>Kenema, Sierra Leone</td>
<td>74%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sept.-Oct., 2014**</td>
<td>151</td>
<td>Freetown, Sierra Leone</td>
<td>48%</td>
<td>-35%</td>
<td>-35%</td>
</tr>
<tr>
<td>Oct.-Nov., 2014**</td>
<td>126</td>
<td>Freetown, Sierra Leone</td>
<td>32%</td>
<td>-33%</td>
<td>-55%</td>
</tr>
<tr>
<td>Nov.-Dec., 2014**</td>
<td>304</td>
<td>Freetown, Sierra Leone</td>
<td>23%</td>
<td>-28%</td>
<td>-69%</td>
</tr>
</tbody>
</table>

Challenges (1)

- Lack of a robust health care system
- Lack of a established institutions (FDA, IRBs, academic centers) for conducting programs of human subjects research
- Limited workforce with appropriate training
- A rapidly evolving epidemic from the perspectives of incidence and medical management
Challenges (2)

- Multiple entities working in environments with limited “bandwidth” vying for the same limited resources.
- A urgent desire to do “something” potentially taking precedence over doing things the right way.
- Media distortions
- Public health interpretation of results, how to use a safe, immunogenic vaccine with NHP efficacy data?
Opportunities

- To build clinical research programs in accordance with high scientific, operational and ethical standards and by extension enhance the healthcare systems they support.

- To do things in a rigorous fashion from the beginning to insure that we leave this epidemic with more knowledge than we had when we entered it.

- To coordinate activities among the various countries and agencies working in West Africa to make sure that the most scientifically sound studies with the greatest potential impact are given priority.