EBOLA VACCINES UPDATE

Gary L. Disbrow, Ph.D.
September 9, 2015
Development and Evaluation of Ebola Vaccines Has Been a Coordinated Effort

- **Development**
  - NIH
  - DoD
  - BARDA
  - FDA
  - PHAC
  - Industry partners

- **Evaluation**
  - NIH
  - DoD
  - CDC/OID/NCIRD
  - FDA
  - BARDA
  - WHO
  - NGOs
  - Industry partners
  - Liberia, Sierra Leone, and Guinea regulatory authorities
Ebola Vaccine Landscape

Summer 2014

**PHASES**

- **Discovery**
  - VEE Replicon and VLP
  - Self-amplifying RNA vaccine
  - HuAd5 TRL3 agonist
- **Preclinical Development**
  - rVSVN4CT1
  - HuAd26/MVA
  - ChAd3
  - EBOV GP Nanoparticle
  - Rabies EBOV
  - NOVAVAX
  - NewLink Genetics
- **Phase I**
- **Phase II**
- **Phase III**

**Companies**

- Prefectus BioSciences, Inc.
- Crucell
- Bavarian Nordic
- GSK
- Jefferson
- Vaxart
- NOVARTIS
Ebola Vaccine Landscape

**Current**

**Discovery**
- VEE Replicon and VLP
- Self-amplifying RNA vaccine
- HuAd5
- Rabies EBOV

**Preclinical Development**
- rVSVN4CT1
- DNA vaccine
- EBOV GP Nanoparticle
- HuAd26/MVA
- rVSVΔG

**Phase I**
- Crucell
- ChAd3

**Phase II**
- HuAd5
- Influenza vectored vaccine
- Protein Sciences

**Phase III**
- GSK
- Merck

An accessible version can be found on page 14
Three, Large, Phase II/III Vaccine Trials in West Africa

- NIH Sponsored and Supported
- CDC Sponsored
- CDC/BARDA Supported
- WHO, MSF, RC of Norway, PHAC Supported
- MSF, WHO, and Guinea Govt. Sponsored
- Campagne Ebola Ça Suffit
- NIH Sponsored and Supported
Vaccine Trial Guinea

- Newlink/Merck rVSVΔG vaccine
- Open-label, cluster randomized, ring vaccination trial
  - Randomized adult contacts and contacts of contacts of a laboratory confirmed case of Ebola into immediate vaccination or delayed vaccination (21 days), no placebo
  - Assessed Ebola virus disease with onset at least 10 days after randomization
- Preliminary analysis conducted:
  - 48 clusters (4123 individuals) immediate vaccination
    - 0 cases of Ebola
  - 42 clusters (3528 individuals) delayed vaccination
    - 16 cases of Ebola
  - Result suggest efficacy of vaccine and data will be reviewed by regulatory authorities
- Open-label phase IIb trial in healthcare workers evaluating safety and immunogenicity
Vaccine Trial
Sierra Leone

- Newlink/Merck rVSVΔG vaccine
- Unblinded, individually, randomized trial without a placebo arm
- Healthcare and front-line Ebola response workers
  - Randomized to immediate or deferred vaccination (6 months)
- Assessed laboratory confirmed Ebola virus disease, safety, and immunogenicity
  - Over 8700 individuals have been enrolled
  - Immediate vaccination – ~4,150 vaccinated in immediate arm
  - Delayed vaccination – will begin in September
    - Reactogenicity in subgroup (~400 patients/group)
    - Immunogenicity in subgroup (~500 patients)
Vaccine Trial
Liberia

- Newlink/Merck rVSVΔG and GSK ChAd3 vaccines
- Randomized, double-blinded, placebo controlled trial
  - Evaluate safety, efficacy, and immunogenicity of the vaccine candidates
- Healthy adults or individuals at risk for EVD
  - 500 individuals in each of three arms
- Enrollment and vaccination is complete
  - Lack of Ebola disease – unable to evaluate efficacy of the vaccines
Safety and Immunogenicity

- Newlink/Merck rVSVΔG – $2 \times 10^7$
- In general, the vaccine appears to be safe and well tolerated
  - Multiple doses have been evaluated – $3 \times 10^3$ – $1 \times 10^8$
  - Vaccine has been administered to ~14,000 individuals
    - Has been administered to 20 individuals 13-17 and 20 individuals 6-12 yrs of age (Gabon) with no reported SAEs
- Reports of arthralgia/arthritis resulted in pausing of a Phase I trial
- One vaccine related SAE reported in the Guinea trial
- Immunogenicity results will be forthcoming
Safety and Immunogenicity

- GSK ChAd3 – $1 \times 10^{11}$
- In general, the vaccine appears to be safe and well tolerated
  - Multiple doses have been evaluated – $1 \times 10^{10} – 2 \times 10^{11}$ (bivalent vaccine)
  - No reports of administration to pediatric patients
  - Immunogenicity results will be forthcoming
Vaccine Trial Challenges

- Balancing establishing/running a clinical trail during an international response to an epidemic
- Cold chain issues and lack of infrastructure
- There has been a rapid decrease in the number of Ebola cases
  - A good thing
- Adapting to cultural, educational, and language differences
- Lack of previous clinical trial experience in West Africa
  - Health care workers and volunteers are/were enthusiastic to help conduct the trials
- Follow-up and tracking of trial participants
What’s Next

- BARDA is currently supporting three vaccine candidates with a fourth under consideration
  - Working in collaboration with DoD and NIH
- BARDA funding was provided under an Ebola CR and Supplemental
  - FY 2016 funding is uncertain above base ARD funding
  - Potential for vaccines/therapeutics to transition to PBS in FY16-17
- BARDA is supporting manufacturing for clinical trails, scale-up manufacturing, enhanced formulation
- Current vaccine candidates are monovalent, both DoD and HHS have an objective to develop trivalent vaccines
- Who will support manufacturing if a mass vaccination campaign is implemented?
- How will regulatory authorities license vaccines in the absence of definitive or sufficient efficacy data?
  - Animal rule
  - Accelerated approval pathway
DISCUSSION
## Ebola Vaccine Landscape

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<th>Vaccine</th>
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