



EBOLA VACCINES UPDATE

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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



VEE Replicon and VLP



Profectus BioSciences, Inc.
rVSVN4CT1



BAVARIAN NORDIC

HuAd26/MVA



Self-amplifying RNA vaccine



HuAd5 TRL3 agonist



Rabies EBOV



ChAd3



rVSVΔG



EBOV GP Nanoparticle



Ebola Vaccine Landscape

Current



VEE Replicon and VLP

rVSVN4CT1



ChAd3



Self-amplifying RNA vaccine



BAVARIAN NORDIC

HuAd26/MVA



rVSVΔG



HuAd5



Rabies EBOV

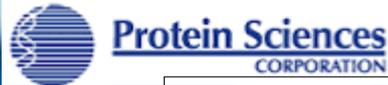
EBOV GP Nanoparticle



Influenza vectored vaccine



HuAd5



GP subunit



MVA based boost

An accessible version can be found on page 14

Creating Tomorrow's Vaccines

Three, Large, Phase II/III Vaccine Trials in West Africa



Campagne Ebola Ça Suffit

MSF, WHO, and Guinea Govt. Sponsored
WHO, WT, MSF, RC of Norway, PHAC
Supported



CDC Sponsored
CDC/BARDA Supported



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)



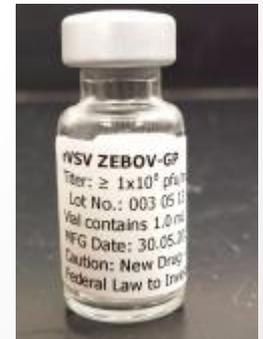
Vaccine Trial Liberia

- Newlink/Merck rVSV Δ G 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



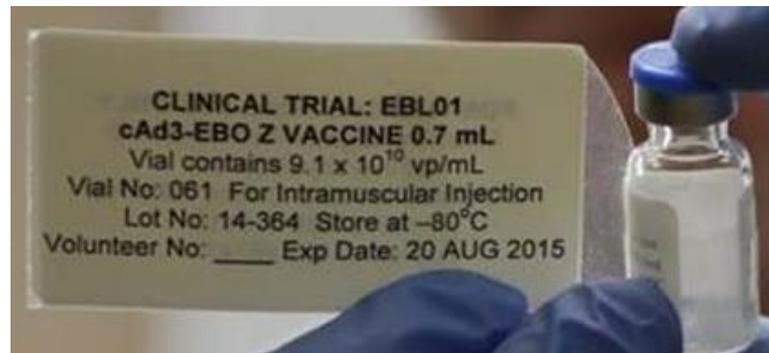
Safety and Immunogenicity

- Newlink/Merck rVSVΔG – 2×10^7
- In general, the vaccine appears to be safe and well tolerated
 - Multiple doses have been evaluated – 3×10^3 – 1×10^8
 - 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 – 1×10^{11}
- In general, the vaccine appears to be safe and well tolerated
 - Multiple doses have been evaluated – 1×10^{10} – 2×10^{11} (bivalent vaccine)
 - No reports of administration to pediatric patients
 - Immunogenicity results will be forthcoming



Vaccine Trial Challenges

- Balancing establishing/running a clinical trial 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 trials, 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

Company	Vaccine	Summer 2014 Status	Current Status
USAMRID	VEE Replicon and VLP	Discovery	Discovery
NOVARTIS	Self-amplifying RNA vaccine	Discovery	Discovery
VAXART	HuAd5 TRL3 agonist	Discovery	Discovery
PBS(Profectus BioSciences, Inc	rVSVN4CT1	Preclinical Development	Preclinical Development
Inovio	DNA vaccine	Preclinical Development	Preclinical Development
Jefferson	Rabies EBOV	Preclinical Development	Preclinical Development
NOVAVAX	EBOV GP Nanoparticle	Preclinical Development	Phase I
Crucell, Bavarian Nordic	HuAd26/MVA	Phase 1	Phase I
Gsk	ChAd3	Phase 1	Phase II
NewLink Genetics	rVSVAG	Phase1	Phase III
Protein Sciences Corporation	GP Subunit		Preclinical Development
Emergent Biosolutions	MVA based boost		Preclinical Development
Chinese Center for Disease Control and Prevention	HuAd5		Phase I
MNHNCTEPCTBO	Influenza vectored vaccine		Discovery
Merck	rVSV-ZEBOV-GP		Phase III