WELLCOME TRUST-CIDRAP EBOLA VACCINE TEAM B

EBOLA VACCINE CLINICAL TRIALS

Situation Update – Revised August 2015

This situation update summarizes the clinical trials that have been registered and initiated for assessing or comparing the safety, immunogenicity, and/or efficacy of the following current Ebola vaccine candidates:

- Recombinant Chimpanzee Adenovirus Type 3–Vectored Vaccine (cAd3-EBO and cAd3-EBOZ) with or without Modified Vaccinia Virus Ankara-Bavarian Nordic (MVA-BN®) Filo-vector Vaccine
- Recombinant Vesicular Stomatitis Virus-based Vaccine (rVSVΔG-ZEBOV)
- Adenovirus Type-26 Vector-based Vaccine (Ad26.ZEBOV) with MVA-BN® Filo
- Recombinant Human Type 5 Adenovirus Vector-based Vaccine (Ad5-EBOV)
- Glycoprotein Nanoparticle Vaccine (EBOV GP) with or without Matrix-M™ Adjuvant
- DNA vaccine INO-4212

We identified a total of 35 clinical trials involving the vaccine candidates listed above, as of August 8, 2015. The trials include those that are currently recruiting participants, ongoing but no longer recruiting participants, about to begin recruiting participants, or just recently completed. Clinical trials conducted on previous Ebola vaccine candidates evaluated before 2014 and no longer being developed are not included. Information on these trials was obtained from the following registries:

- The National Institutes of Health ClinicalTrials.gov (https://clinicaltrials.gov)
- The Pan African Clinical Trials Registry (http://www.pactr.org)
- The World Health Organization International Clinical Trials Registry Platform (http://apps.who.int/trialsearch)

The information gathered from these registries may not necessarily include all clinical trials being conducted and also may not reflect current status. We plan to update this summary as additional information becomes available in the clinical trial registries and published literature. This document will also be posted on the Ebola Vaccine Team B Web site.

KEY FINDINGS

- **PHASE 1 OR 1/2 TRIALS**

  Twenty-seven of the studies involve phase 1 or phase 1/2 trials aimed at assessing vaccine safety (including reactogenicity) and immunogenicity.

  - *Location.* These trials are taking place in 15 countries: United States (7), United Kingdom (4), China (2), Mali (2), Switzerland (2), Uganda (2), Australia (1), Canada (1), Gabon (1), Germany (1), Ghana (1), Kenya (1), Senegal (1), Sierra Leone (1), and Tanzania (1).
  - *Blood.* Most of the trials involve obtaining blood specimens to assess various immunologic responses to vaccination (including measures of humoral and cellular immunity).

- *Age*. Most of the trials involve persons at least 18 years old; 2 trials involve children (in Sierra Leone and Gabon).

- **PHASE 2 TRIALS**

  Four of the studies involve phase 2 trials aimed at evaluating safety and immunogenicity in larger study populations.

  - *Location.* These trials are taking place in 7 countries: Senegal (3), Cameroon (2), Ghana (2), Mali (2), Nigeria (2), France (1), and the United Kingdom (1).
  - *Age.* Most of the trials involve persons at least 18 years old; 1 trial involves children (in Mali and Senegal).

- **PHASE 2/3 OR 3 TRIALS**

  Four clinical trials—two phase 2/3 and one phase 3–have been initiated in 3 countries in Africa (Liberia, Sierra Leone, and Guinea) and a fourth trial (phase 3) has been registered but not yet initiated (unspecified location).

  - *Liberia*. The Liberia trial, sponsored by the US National Institute of Allergy and Infectious Diseases (NIAID), is a phase 2/3 trial examining safety and efficacy of two candidate vaccines (cAd-EBOZ and VSVΔG-ZEBOV). The plan is to enroll 600 adults as part of a phase 2 safety and immunogenicity study, with blood draw for immunogenicity testing. As originally planned, the phase 2 study was to be followed by a phase 3 efficacy study involving an additional 27,570 participants. The phase 3 portion of this trial in Liberia was been suspended in April 2015 due to the low incidence of Ebola virus disease (EVD) in Liberia.
  - *Sierra Leone.* The Sierra Leone trial, sponsored by the US Centers for Disease Control and Prevention (CDC), is a phase 2/3 safety and efficacy study involving a single dose of rVSVΔG-ZEBOV. This trial is ongoing and intends to enroll about 6,000 frontline workers in a phased rollout, with 3,000 workers randomized to receive immediate vaccination and 3,000 randomized to receive delayed vaccination (18 to 24 weeks after enrollment).
  - *Guinea.* The Guinea trial, sponsored by the World Health Organization (WHO), is a phase 3 trial involving the rVSVΔG-ZEBOV vaccine. Preliminary results, published July 31, 2015, in the Lancet by Henao-Restrepo, et al suggest that rVSV-ZEBOV might be highly efficacious and safe in preventing EVD (see summary below on page 5).

- **PUBLISHED REPORTS**

  Six reports involving Ebola vaccine clinical trials have been published to date. (The information below is taken from the publication abstracts.)

  1. **Ledgerwood JE, et al**

     The report summarizes a phase 1, dose-escalation, open-label trial of cAd3-EBO involving 20 subjects. Subjects received either a 2×10^{10} particle-unit dose or a 2×10^{11} particle-unit dose.

- *No safety concerns were identified*; however, transient fever developed within 1 day after vaccination in two participants who had received the 2×10^{11} particle-unit dose.
- *Glycoprotein-specific antibodies* were induced in all 20 participants; the titers were of greater magnitude in the group that received the 2×10^{11} particle-unit dose than in the group that received the 2×10^{10} particle-unit dose (geometric mean titer against the Zaire antigen, 2037 vs. 331; P=0.001).
- *Glycoprotein-specific T-cell responses* were more frequent among those who received the $2x10^{11}$ particle-unit dose than among those who received the 2×10^{10} particle-unit dose, with a CD4 response in 10 of 10 participants versus 3 of 10 participants (P=0.004) and a CD8 response in 7 of 10 participants versus 2 of 10 participants (P=0.07).
- The authors concluded that reactogenicity and immune responses to cAd3-EBO vaccine were dose-dependent. At the 2×10^{11} particle-unit dose, glycoprotein Zaire–specific antibody responses were in the range reported to be associated with vaccine-induced protective immunity in challenge studies involving nonhuman primates.

2. **Rampling T, et al**

   Sixty healthy adult volunteers in Oxford, United Kingdom, received a single dose of the cAd3 vaccine at one of three dose levels: 1×10^{10} viral particles, 2.5×10^{10} viral particles, and 5×10^{10} viral particles (with 20 participants per group).
   - *No safety concerns were identified* during a 4-week follow-up period.
   - *Fever developed* in 2 of the 59 participants who were evaluated.
   - *Prolonged activated partial-thromboplastin times and transient hyperbilirubinemia* were observed in 4 and 8 participants, respectively.
   - *Geometric mean antibody responses* on ELISA were highest (469 units; range, 58 to 4051; 68% response rate) at 4 weeks in the high-dose group, which had a 100% response rate for T cells on ELISpot, peaking at day 14 (median, 693 spot-forming cells per million peripheral-blood mononuclear cells).
   - *At the vaccine doses tested, both antibody and T-cell responses were detected*, but at levels lower than those induced in macaques protected by the same vaccine.

3. **Regules JA, et al**

   Two phase 1, placebo-controlled, double-blind, dose-escalation trials were conducted of an rVSVΔG-ZEBOV vaccine (conducted in Bethesda and Silver Spring, MD, USA). Twenty-six adults at each site (52 participants) were consecutively enrolled into groups of 13 each. Three volunteers in each group received an intramuscular injection of placebo, and 10 received an intramuscular injection of the rVSVΔG-ZEBOV vaccine at a dose of either 3 million plaque-forming units (PFU) or 20 million PFU.

- *No safety concerns were identified*; the most common adverse events were injection-site pain, myalgia, and fatigue.
- *Transient VSV viremia was noted* in all the vaccine recipients. By day 28, all the vaccine recipients had seroconversion as assessed by an ELISA against the glycoprotein of the ZEBOV-Kikwit strain.
- *At day 28, geometric mean titers of antibodies* against ZEBOV glycoprotein were higher in the group receiving 20 million PFU than in the group receiving 3 million PFU, as assessed by ELISA (geometric mean antibody titer, 4079 vs. 1300; P<0.001) and by pseudovirion neutralization assay (geometric mean antibody titer, 441 vs. 223; P=0.07).

4. **Agnandji ST, et al**

   Three open-label, dose-escalation phase 1 trials and one randomized, double-blind, controlled phase 1 trial were performed to assess safety, side-effect profile, and immunogenicity of rVSVΔG-ZEBOV at various doses in 158 healthy adults in Europe and Africa (study sites included Kilifi, Kenya; Hamburg, Germany; Lambaréné, Gabon; and Geneva, Switzerland). Participants were injected with doses of vaccine ranging from 300,000 to 50 million plaque-forming units (PFU) or placebo.

   - *No serious vaccine-related adverse events* were reported.
   - *Mild-to-moderate early-onset reactogenicity* was frequent but transient (median, 1 day). Fever was observed in up to 35% of vaccinees.
   - *Vaccine viremia* was detected within 3 days in 103 of 110 participants (94%) receiving 3 million PFU or more; rVSV was not detected in saliva or urine.
   - *In the second week after injection, arthritis affecting one to four joints* developed in 11 of 51 participants (22%) in Geneva, with pain lasting a median of 8 days; 2 self-limited cases occurred in 40 participants (5%) in Hamburg, Germany, and Kilifi, Kenya.
   - *The virus was identified in one synovial-fluid aspirate and in skin vesicles* of 2 other vaccinees, showing peripheral viral replication in the second week after immunization.
   - *ZEBOV-glycoprotein–specific antibody responses* were detected in all the vaccinated participants, with similar glycoprotein-binding antibody titers but significantly higher neutralizing antibody titers at higher doses.

5. **Zhu FC, et al**

   Between Dec 28, 2014, and Jan 9, 2015, 120 healthy adult participants were enrolled and randomly assigned to receive placebo (n=40), low-dose vaccine (n=40), or high-dose adenovirus type-5 vector-based Ebola vaccine. Participants were followed up for 28 days.

   - *Overall, 82 (68%) participants reported at least one solicited adverse reaction* within 7 days of vaccination (n=19 in the placebo group *vs* n=27 in the low-dose group *vs* n=36 in the high-dose group; p=0.0002).

- *The most common reaction was mild pain at the injection site*, which was reported in eight (20%) participants in the placebo group, 14 (35%) participants in the low-dose group, and 29 (73%) participants in the high-dose vaccine group ($p<0.0001$).
- *No serious adverse events were noted*.
- *Glycoprotein-specific antibody titers* were detected in participants in the low-dose and high-dose vaccine groups at both day 14 and day 28.
- *T-cell responses* peaked at day 14 at a median of 465 spot-forming cells in participants in the low-dose group and 765 cells in those in the high-dose group.

6. **Henao-Restrepo, et al**

In a phase 3, open-label, cluster-randomized ring vaccination trial, suspected cases of EVD in Basse-Guinée (Guinea, West Africa) were independently ascertained by Ebola response teams as part of a national surveillance system. After laboratory confirmation of a new case, clusters of all contacts and contacts of contacts were defined and randomly allocated 1:1 to immediate vaccination or delayed (21 days later) vaccination with rVSV-ZEBOV (one dose of 2×10^7 pfu). The primary analysis compared the incidence of EVD in eligible and vaccinated individuals in immediate vaccination clusters with the incidence in eligible individuals in delayed vaccination clusters. Between April 1, 2015, and July 20, 2015, 90 clusters, with a total population of 7651 people were included in the planned interim analysis; 48 of these clusters (4123 people) were randomly assigned to immediate vaccination with rVSV-ZEBOV, and 42 clusters (3528 people) were randomly assigned to delayed vaccination with rVSV-ZEBOV. Based on an interim analysis, the following results were reported:

- *In the immediate vaccination group, there were no cases of EVD with symptom onset at least 10 days after randomization, whereas in the delayed vaccination group there were 16 cases of EVD from seven clusters*, showing a vaccine efficacy of 100% (95% CI 74.7–100.0; p=0.0036).
- *43 serious adverse events were reported*; one serious adverse event was judged to be causally related to vaccination (a febrile episode in a vaccinated participant, which resolved without sequelae); assessment of serious adverse events is ongoing.
- *rVSV-ZEBOV might be highly efficacious and safe in preventing EVD*, and is most likely effective at the population level when delivered during an EVD outbreak via a ring vaccination strategy.

7. **Huttner, et al**

To evaluate safety and immunogenicity of various doses of the rVSV vaccine, a phase 1/2, dose-finding, placebo-controlled, double-blind trial was conducted at the University Hospitals of Geneva, Switzerland, enrolling non-pregnant, immunocompetent, and otherwise healthy adults ages 18 to 6. Huttner et al. 2015 reported safety and immunogenicity results in volunteers receiving low dose (3×10^5 pfu) rVSV vaccine

compared with volunteers who had received higher doses (1×10^7 pfu or 5×10^7 pfu) or placebo before a safety-driven study hold. Results showed that reducing the dose of rVSV-ZEBOV from $1–5 \times 10^7$ to 3×10^5 pfu was associated with the following outcomes:

- Decreases in the occurrence and magnitude of viremia, monocyte activation, and early reactogenicity
- Negative effects on antibody responses
- Failure to prevent viral seeding of peripheral tissues
- No decrease the risk of vaccine-induced arthritis, dermatitis, and cutaneous vasculitis.

The authors concluded that administering low dose rVSV-ZEBOV is not a useful strategy to prevent vaccine-induced arthritis, dermatitis, or vasculitis.

- **SUMMARY TABLES**

Information about the 35 identified trials is summarized in the following tables (beginning on page 8):

- **EDITORIAL**

In addition to publications on specific vaccine trials, an editorial about Ebola vaccines was published online in the *Lancet* on April 3, 2015 (Heymann DL, et al. *Ebola vaccines: keep the clinical trial protocols on the shelf and ready to roll out*). The authors raise points regarding:

- *Preparedness.* The authors make a number of key points about use of Ebola virus vaccines and emphasize the need to be proactively prepared for future Ebola outbreaks.
- *Efficacy.* The authors raise the concern that current phase 3 trials may not have sufficient power to demonstrate vaccine efficacy if/as incidence continues to wane as hoped.
- *Resuming trials*. To address the efficacy issues, the authors argue that Ebola vaccine trials should be able to resume rapidly if necessary when and where the next Ebola outbreak occurs. This will require a concerted effort involving the WHO; regulatory

agencies in Africa, the United States, and Europe; and other key partners to address the following issues:

- *Stockpiling.* Vaccines already produced must be stockpiled and maintained in sufficient quantities for future clinical trials.
- *Funding.* Funders of clinical trials must maintain fluid funding to roll out trial operations when new outbreaks occur.
- *Clearances.* Countries at risk of Ebola outbreaks must provide ethical, regulatory, and other clearances in the period between outbreaks and maintain these clearances until future outbreaks occur.
- *Protocols.* Scientists must ensure that clinical trial protocols are ready to rapidly implement when needed.

The authors also suggest that given the declining incidence of EVD, regulatory agencies should develop an accelerated licensure strategy for Ebola vaccines based primarily on safety and immunogenicity (serologic correlates of protection) in relevant human populations, rather than relying on direct evidence of vaccine efficacy, provided that confirmatory trials to establish vaccine efficacy are conducted after vaccine licensure and registration. Such an approach would permit registration and stockpiling of one or more Ebola vaccines during the next 12 to 18 months, thereby facilitating the introduction of a vaccine for further safety and efficacy evaluation in the event of a new outbreak.

Table 1. Chimpanzee Adenovirus3 (cAd3) (*GlaxoSmithKline*) with or without MVA-BN® Filo (*Bavarian Nordic*)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[1] *VRC 207: A Phase 1/1b, Open-Label, Dose-Escalation Clinical Trial to Evaluate the Safety, Tolerability and Immunogenicity of the Ebola Chimpanzee Adenovirus Vector Vaccines, VRC-EBOADC069-00-VP (cAd3-EBO) and VRC-EBOADC076-00-VP (cAd3-EBOZ), in Healthy Adults* NCT02231866 NIAID-sponsored Decatur GA, Baltimore MD, Bethesda MD, USA Started Aug 2014	Single dose of cAd3-EBO or cAd3-EBOZ Phase 1/1b: Safety, reactogenicity and immunogenicity (antibody and T-cell responses)	Nonrandomized, open-label Dose escalation and evaluation of Zaire component • Part 1: enroll 20 subjects with 10 in each of the two dosage groups for cAd3-EBO (ages 18-50 years) • Part 2: enroll 130 subjects (ages 18-65 years) Antibody response and T-cell responses will be assessed	Active; not recruiting participants (Registry last updated: June 6, 2015) Ledgerwood JE et al. Chimpanzee Adenovirus Vector Ebola Vaccine—Preliminary Report. *New Engl J Med* 2014 Nov 26 [Text]
[2] *VRC 208: Phase 1/1b Open-Label Clinical Trial to Evaluate Dose, Safety & Amp; Immunogenicity of Recombinant Modified Vaccinia Virus Ankara Ebola Vaccine,VRC-EBOMVA079-00-VP, Administered Alone or as Boost to cAd3-Ebola Vaccines in Healthy Adults* NCT02408913 NIAID-sponsored USA (GA, MD) Started Mar 2015	MVA-EbolaZ or as a boost to cAd3-Ebola vaccine Phase 1/1b: Dose, safety, tolerability and immunogenicity (antibody and T-cell responses)	Randomized, open-label Dose escalation Enroll 160 adults (ages 18-50 years) • Part 1: vaccine-naive subjects; dose escalation of the MVA-EbolaZ vaccine and evaluation as a boost for the cAd3-EBO vaccine • Part 2: up to 140 subjects who received the cAd3-EBO or cAd3-EBOZ vaccine in VRC 207 study will be boosted with MVA-EbolaZ Antibody and T-cell responses will be assessed	Recruiting participants (Registry last updated: May 13, 2015)
[3] *A Phase 1B, Open-label, Clinical Trial to Evaluate Safety, Tolerability and Immunogenicity of Ebola Chimpanzee Adenovirus Vector Vaccines VRC-EBOADC069-00-VP and VRC-EBOADC076-00-VP, in Healthy Adults in Kampala, Uganda* *Protocol RV 422* NCT02354404 PACTR201412000957310	cAd3-EBO, cAd3-EBOZ Phase 1b: Safety, tolerability and immunogenicity (cellular and humoral)	Randomized, open-label Enroll 90 healthy adults (ages 18-65 years) • Group 1: at least 60 volunteers who have never received an investigational Ebola vaccine • Group 2: up to 30 eligible participants who previously participated in the RV 247 vaccine clinical trial and received the investigational VRC-EBODNA023-	Active; not recruiting participants (Registry last updated: July 22, 2015)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
NIAID-sponsored Kampala, Uganda Started Jan 2015		00-VP (Ebola DNA WT) vaccine Antibody and T-cell responses will be assessed	
[4] *A Phase 1a, Dose-Escalating, Safety and Immunogenicity Trial of the Monovalent Zaire Ebola Viral Vector Candidate Vaccine cAd3-EBO Z and the Heterologous Prime-boost Candidate Vaccine Regimen cAd3-EBO Z and MVA-BN® Filo in Healthy UK Adults* NCT02240875 Univ. of Oxford-sponsored UK Start Sep 2014	cAd3-EBO Z MVA-BN® Filo Phase 1: safety, tolerability and immunogenicity (cellular and humoral)	Nonrandomized, open-label Dose escalation (cAd3-EBO Z at 3 different doses, and a second vaccine, MVA-BN® Filo, at 3 different doses) Some subjects will receive only cAd3-EBO Z and some will also receive MVA-BN® Filo Enroll 92 adults (ages 18-50 years) Antibody and T-cell responses will be assessed	Recruiting participants (Registry last updated: June 18, 2015) Rampling T et al. A Monovalent Chimpanzee Adenovirus Ebola Vaccine—Preliminary Report. *New Engl J Med* 2015 Jan 28 [Text]
[5] *A Phase 1b, Dose-escalating Safety and Immunogenicity Trial of the Novel Monovalent Ebola Zaire Candidate Vaccine, cAd3-EBO Z and the Heterologous Prime-boost Candidate Vaccine Regimen of cAD3-EBO Z Followed by MVA-BN® Filo in Malian Adults Aged 18-50 Years* NCT02267109 University of Maryland-sponsored Bamako, Mali Started Oct 2014	cAd3-EBO Z MVA-BN® Filo Phase 1b: safety, reactogenicity and immunogenicity (cellular and humoral)	Nonrandomized, open-label, placebo-controlled Dose escalation at 4 doses Enroll 91 healthy adults (ages 18-50 years) Antibody and T-cell responses will be assessed	Ongoing but not recruiting participants (Registry last updated: June 17, 2015)
[6] *A Phase 1b, Double-blind, Clinical Trial to Evaluate the Safety, Tolerability and Immunogenicity of Two Different Dosage Levels of Ebola Chimpanzee Adenovirus Vector Vaccine "VRC-EBOAdc069-00-vp (cAd3-EBO)" and the Heterologous Prime-Boost Candidate Vaccine Regimen of cAd3-EBO Followed by MVA-Vectored Vaccine in Healthy Adults, 18-65 Years of Age, in Bamako, Mali*	cAd3-EBO bivalent vaccine (Zaire plus Sudan) MVA-EbolaZ (booster) Phase 1b: safety, reactogenicity, immunogenicity	Randomized, double-blind Two dose levels of bivalent vaccine Participants in each group will be randomized to receive the candidate booster vaccine MVA-EbolaZ or placebo to be completed 4 to 16 weeks after priming	Currently recruiting participants (Registry last updated: June 24, 2015)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
NCT02368119 University of Maryland-sponsored Bamako, Mali Started Feb 2015		dose Enroll 60 healthy adults (ages 18-65) Antibody and T-cell responses will be assessed	
[7] *A Phase 1/2 Double-blind, Randomized, Placebo Controlled, Safety and Immunogenicity, Dose-finding Trial of the Monovalent Zaire Ebola Chimpanzee Adenovirus Vector Candidate Vaccine cAd3-EBOZ in Healthy Adults in Switzerland* NCT02289027 Centre Hospitalier Universitaire Vaudois-sponsored Lausanne, Switzerland Started Oct 2014	cAd3-EBOZ Phase 1/2: safety, reactogenicity, immunogenicity	Randomized, double-blind, placebo-controlled Two dose levels Enroll 120 healthy adults (ages 18-65 years), "possibly exposed volunteers" who anticipate deployment to epidemic areas of Africa and "not exposed volunteers" (no planned deployment to the epidemic zone) Antibody and T-cell responses will be assessed	Study completed (Registry last updated: July 24, 2015)
[8] *A Phase Ib Safety and Immunogenicity Clinical Trial of Heterologous Prime-boost Immunization With ChAd3-EBO Z and MVA-EBO Z in Healthy Senegalese Adult Volunteers Aged 18-50 Years* NCT02485912 University of Oxford-sponsored Dakar, Senegal Started July 2015	ChAd3-EBO Z MVA-EBO Z Phase 1b: safety, immunogenicity	Randomized, open-label All volunteers receive a ChAd3-EBO Z priming vaccine and then MVA-EBO Z boosting vaccine 7 days later; the site of administration of the MVA-EBO Z vaccine differs between the two groups (randomized to the same or opposite arm as the ChAd3-EBO Z vaccine) Enroll 40 healthy adults (ages 18-50 years) Immune responses will be measured by tests on blood samples.	Currently recruiting participants (Registry last updated: July 8, 2015)

[9] *A Phase Ia Clinical Trial to Assess the Safety and Immunogenicity of MVA-EBO Z Alone and a Heterologous Prime-boost Immunization With ChAd3-EBO Z and MVA-EBO Z in Healthy UK Volunteers* NCT02451891 University of Oxford-sponsored Oxford and London, UK Started April 2015	MVA-EBO Z (alone) cAd3-EBO Z then MVA EBO Z Phase 1a: safety, immunogenicity Immune responses will be measured by tests on blood samples	Non-randomized, open-label Group 1: Given MVA-EBO Z vaccine only Groups 2, 3 and 4: Given cAd3-EBO Z followed by the boost vaccine, MVA EBO Z, with booster vaccine given at different doses and days following administration of cAd3-EBO Z. Enroll 38 health adults (ages 18-50 years)	Currently recruiting participants (Registry last updated: May 19, 2015)
[10] *Safety and Immunogenicity Study of GSK Biologicals' Investigational Recombinant Chimpanzee Adenovirus Type 3-vectored Ebola Zaire Vaccine (GSK3390107A) in Adults in Africa* NCT02485301 GlaxoSmithKline-sponsored Senegal Started July 2015	ChAd3-EBO-Z Phase 2: safety and immunogenicity Anti-GP EBOV antibody titers measured by enzyme-linked immunosorbent assay (ELISA)	Randomized, double-blind, placebo-controlled • Group EBO-Z will receive the vaccine at Day 0 of the study • Group Placebo/EBO-Z will receive a placebo at Day 0 (as a control) and the ChAd3-EBO-Z vaccine 6 months later Enroll 2796 health adults (18 years or older)	Not yet open for recruitment (Registry last updated: July 16, 2015)
[11] *202091 (EBOLA Z CHAD3-005)* PACTR201504001092179 GlaxoSmithKline-sponsored Mali, Ghana, Nigeria, Senegal, Cameroon Start August 15, 2015	cAd3-EBO-Z Phase 2: Safety, reactogenicity, and humoral immunogenicity Anti-GP EBOV antibody titers measured by ELISA	Randomized, double-blind, placebo-controlled Enroll 3000 healthy adults living in countries adjacent to the current Ebola outbreak	Not yet recruiting Registered April 1, 2015
[12] *202090 (EBOLA Z CHAD3-004)* PACTR201507001154522 GlaxoSmithKline-sponsored Mali, Ghana, Nigeria, Senegal, Cameroon	cAd3 EBO-Z Nimenrix Meningococcal vaccine (GSK) Phase 2: safety and immunogenicity in children	Randomized, controlled trial, stratified by age • Experimental group: Receive cAd3 EBO-Z at day 0 and Nimenrix at month 6. • Control group: Receive Nimenrix at day 0 and cAd3 EBO-Z at month 6	Not yet recruiting Registered June 1, 2015 EBOLA Z CHAD3-005 (listed above) will start before EBOLA Z CHAD3-004 to collect safety and reactogenicity data in

Start August 15, 2015		Enroll 600 healthy children (ages 1-17) living in countries adjacent to the current Ebola outbreak zones.	100 adults, after 1 week of follow-up, living in countries adjacent to the current Ebola outbreak, before proceeding to vaccination of children.

Table 2. Replication-Competent Recombinant Vesicular Stomatitis Virus (rVSV)-Based Ebola Vaccine (*Merck/NewLink Genetics*)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[13] *A Phase 1 Randomized, Double-Blind, Placebo Controlled, Dose-Escalation Study to Evaluate the Safety and Immunogenicity of Prime-Boost VSV Ebola Vaccine in Healthy Adults* NCT02280408 NewLink Genetics-sponsored Bethesda MD, USA Started Aug 2014	rVSVΔG-ZEBOV Phase 1: safety, immunogenicity	Randomized, double-blind, placebo-controlled 3-arm, dose escalation Enroll 120 healthy adults (ages 18-65 years) Immunogenicity will be measured by ELISA and neutralization	Ongoing but not recruiting participants (Last verified on ClinicalTrials.gov Jan 2015) Regules JA, et al. A Recombinant Vesicular Stomatitis Virus Ebola Vaccine—Preliminary Report. *New Engl J Med*, published online April 1, 2015 [link]
[14] *A Phase 1 Randomized, Single-Center, Double-Blind, Placebo Controlled, Dose-Escalation Study to Evaluate the Safety and Immunogenicity of the BPSC-1001 (VSVΔG-ZEBOV) Ebola Virus Vaccine Candidate in Healthy Adult Subjects* NCT02269423 NewLink Genetics-sponsored Silver Spring, MD, USA Started Oct 2014	rVSVΔG-ZEBOV Phase 1: safety, immunogenicity	Randomized, double-blind, placebo-controlled 3-arm, dose escalation Enroll 117 healthy adults (ages 18-50 years) Immunogenicity will be assessed by cross-reactive antibody response, immune response in the context of HLA allele expression, and Ig production; vaccine viremia also will be measured	Ongoing but not recruiting participants (Last verified on ClinicalTrials.gov Jan 2015) Regules JA, et al. A Recombinant Vesicular Stomatitis Virus Ebola Vaccine—Preliminary Report. New Engl J Med, published online April 1, 2015 [link]
[15] *A Phase 1, Open-Label, Dose-Escalation Study to Evaluate the Safety and Immunogenicity of the BPSC1001 (VSVΔG-ZEBOV) Ebola Virus Vaccine Candidate in Healthy Adult Volunteers in Kilifi, Kenya*. [part of WHO-led VEBCON consortium] NCT02296983 Univ. of Oxford-sponsored Kilifi, Kenya Started Dec 2014	Single dose VSVΔG-ZEBOV Phase 1: safety (AEs, SAEs), tolerability and immunogenicity	Nonrandomized, open-label Dose escalation (two dose levels) Enroll 40 HCWs (ages 18-55 years) Antibody and T-cell responses will be assessed; VSV-ZEBOV viremia and shedding also will be measured	Ongoing but not recruiting participants (Last verified on ClinicalTrials.gov Nov 2014) Agnandji ST, et al. Phase I Trials of rVSV Ebola Vaccine in Africa and Europe—Preliminary Report. *New Engl J Med*, published online April 1, 2015 [link]

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[16] *An Open Label, Single Center, Dose Escalation Phase 1 Trial to Assess the Safety, Tolerability and Immunogenicity of a Single Ascending Dose of the Ebola Virus Vaccine rVSVΔG-ZEBOV-GP (BPSC1001)* [part of WHO-led VEBCON consortium] NCT02283099 Universitätsklinikum Hamburg-Eppendorf-sponsored Hamburg, Germany Started Nov 2014	Single dose rVSVΔG-ZEBOV Phase 1: safety, tolerability and immunogenicity	Single group assignment, open-label Dose escalation (3 cohorts) Enroll 30 adults (ages 18-55 years) Humoral immunity will be assessed; concentration of rVSV will be determined in peripheral blood, urine and saliva as detected by qRT-PCR	Ongoing but not recruiting participants Registry last updated May 6, 2015 Agnandji ST, et al. Phase I Trials of rVSV Ebola Vaccine in Africa and Europe—Preliminary Report. *New Engl J Med*, published online April 1, 2015 [link]
[17] *A Phase 1, Open-Label, Dose-Escalation Study to Evaluate the Safety and Immunogenicity of the BPSC1001 (VSVΔG-ZEBOV) Ebola Virus Vaccine Candidate in Healthy Adult Volunteers in Lambaréné, Gabon.* [part of WHO-led VEBCON consortium] PACTR201411000919191 Universitaetsklinikum Tuebingen-sponsored Lambaréné, Gabon Start Nov 2014	Single dose rVSVΔG-ZEBOV Phase 1: safety, tolerability, reactogenicity, immunogenicity	Group randomization (5 groups), open-label Dose escalation Enrolled 201 participants (6-50 years of age eligible, using age de-escalation to enroll older participants first) Antibody and T-cell responses will be assessed, as will concentration of rVSV in blood, urine or saliva as detected by RT-PCR	Recruiting participants (PACTR accessed on Aug 8, 2015) Agnandji ST, et al. Phase I Trials of rVSV Ebola Vaccine in Africa and Europe—Preliminary Report. *New Engl J Med*, published online April 1, 2015 [link]
[18] *A Phase 1/2 Dose-finding Randomized, Single-center, Double-blind, Placebo-controlled Safety and Immunogenicity Trial of the Vesicular Stomatitis Virus-vectored Zaire Ebola Candidate Vaccine BPSC1001 (VSVΔG-ZEBOV) in Healthy Adults.* [part of WHO-led VEBCON consortium] NCT02287480 University Hospital, Geneva-sponsored Geneva, Switzerland Started Nov 2014	Single dose rVSVΔG-ZEBOV Phase 1/2: safety, tolerability, reactogenicity, immunogenicity	Randomized, double-blind, placebo controlled Dose escalation; 3 doses Enroll 115 adults (ages 18-65 years) Antibody and T-cell responses will be assessed, as will duration of VSVΔG-ZEBOV viremia	Ongoing but not recruiting participants (Last verified on ClinicalTrials.gov Jan 2015) Agnandji ST, et al. Phase I Trials of rVSV Ebola Vaccine in Africa and Europe—Preliminary Report. *New Engl J Med*, published online April 1, 2015 [link] Huttner A, Dayer J-A, Yerly S, et al. The effect of dose on the safety and immunogenicity of the VSV Ebola candidate vaccine: a randomised

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
			double-blind, placebo-controlled phase 1/2 trial. Lancet Infect Dis. Available online 4 August 2015 [Text] Commentary: Ledgerwood JE. Use of low dose rVSV-ZEBOV: safety issues in a Swiss cohort (comment). Lancet Infect Dis. Available online 4 August 2015 [Text]
[19] *A Phase 1 Randomized, Single-Center, Double-Blind, Placebo Controlled, Dose-Ranging Study to Evaluate the Safety and Immunogenicity of the BPSC-1001 (VSVΔG-ZEBOV) Ebola Virus Vaccine Candidate in Healthy Adult Subjects* NCT02374385 Dalhousie University-sponsored Halifax, Nova Scotia, Canada Started Nov 2014	Single dose rVSVΔG-ZEBOV Phase 1: safety (AEs) and immunogenicity	Randomized, single-center, double-blind, placebo-controlled Dose escalation; 3 doses Enroll 40 healthy adults (ages 18-65 years) ZEBOV envelope glycoprotein-specific binding antibody to be measured by ELISA; rVSV in blood, urine, or saliva as detected by real-time polymerase chain reaction [RT-PCR]	Ongoing but not recruiting participants Registry last updated May 13, 2015
[20] *A Phase 1 Randomized, Multi-Center, Double-Blind, Placebo-Controlled, Dose-Response Study to Evaluate the Safety and Immunogenicity of the BPSC-1001 (VSVΔG-ZEBOV) Ebola Virus Vaccine Candidate in Healthy Adult Subjects* December 8, 2014 NCT02314923 NewLink Genetics-sponsored USA (CA, FL, KY, LA, NE, TN, TX) Started Dec 2014	Single dose rVSVΔG-ZEBOV Phase 1: safety (AEs) and Immunogenicity	Randomized, double-blind, placebo-controlled Dose escalation; 4 doses Enroll 320 healthy adults (ages 18-60 years) ZEBOV- specific antibody response and vaccine viremia will be assessed	Ongoing but not recruiting participants Registry last updated May 12, 2015
[21] [*rVSVΔG-ZEBOV] Ebola Prevention Vaccine Evaluation in Sierra Leone* *STRIVE (Sierra Leone Trial to Introduce a Vaccine Against*	Single dose of rVSVΔG-ZEBOV at $2x10^7$ plaque forming units	Unblinded individually randomized to receive immediate vaccination or deferred vaccination (18-24 weeks	Currently recruiting participants Registry last updated July 22, 2015

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
Ebola) NCT02378753 PACTR201502001037220 CDC-sponsored Freetown, Sierra Leone Started Apr 2015	 Phase 2/3: safety(AEs, reactogenicity), efficacy (prevention of laboratory-confirmed EVD)	after enrollment); phased vaccine introduction in the target population Enroll 6000 at-risk persons (HCWs, or surveillance, ambulance, or laboratory personnel responsible for swabbing deceased persons; >18 years of age) Collect and store serum for immunogenicity evaluations and assessment of baseline Ebola IgG antibody levels among a subset of study participants.	CDC press release [Text]
[22] *A Phase III, Randomized, Placebo-Controlled, Clinical Trial to Study the Safety and Immunogenicity of Three Consistency Lots and a High Dose Lot of rVSV-ZEBOV-GP (V920 Ebola Vaccine) in Healthy Adults* NCT02503202 Merck Sharp & Dohme Corp.-sponsored Location not specified Start August 2015	rVSV-ZEBOV-GP Phase 3: safety and immunogenicity of 3 consistency lots and a high-dose lot of rVSV-ZEBOV-GP (V920 Ebola Vaccine); safety evaluated for 6 months post-vaccination	Randomized, double-blind, placebo-controlled Enroll 1125 healthy adults (ages 18-65)	Not yet recruiting Registry last updated July 17, 2015
Abbreviations: AE, adverse events; SAEs, serious adverse events; EVD, Ebola virus disease; HCW, healthcare worker			

Table 3. cAd3 and rVSV Vaccines (*GlaxoSmithKline* and *Merck/NewLink Genetics*)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[23] *Partnership for Research on Ebola Vaccines in Liberia (PREVAIL)* NCT02344407 NIAID-sponsored Monrovia, Liberia Started Jan 2015	Safety and efficacy of two vaccines: cAd3-EBO Z and rVSVΔG-ZEBOV (Doses not specified) Phase 2: safety (AEs), immunogenicity in the first 600 participants (via ELISA and neutralization antigen-specific assays for antibody), and efficacy	Randomized, double-blind, placebo-controlled, 3-arm study Enroll 600 healthy adults (ages ≥18 years) The potential phase 3 portion had planned to enroll 27,570 adults, if no major safety issues were identified in the first 600 participants ELISA and neutralization antigen-specific assays for antibody will be measured for phase 2 participants	Recruiting participants Registry last updated: June 24, 2015 4/16/15 news report indicates that the phase 3 portion of the trial has been suspended owing to a lack of disease occurrence in Liberia [Text]
[24] *A Randomized Trial to Evaluate Ebola Vaccine Efficacy and Safety in Guinea, West Africa* PACTR201503001057193 WHO-sponsored Conakry, Guinea Started Mar 2015	Single dose rVSVΔG-ZEBOV only (Dose not specified) Per additional information from WHO: • Use of rVSVΔG-EBOV (supply available) and cAd3-ZEBOV (as supply becomes available); vaccines to be tested sequentially in two consecutive trials and in different geographic areas • Phase 3: safety (SAEs) and efficacy (prevention of laboratory-confirmed EVD at the level of the ring after 84 days)	Ring vaccination; randomized to immediate vs. delayed vaccination (by 3 weeks); open-label; no placebo Enroll 21,500 adults (individuals aged ≥18 years who are in the defined vaccination ring)	Recruiting participants (PACTR accessed on Aug 8, 2015) Henao-Restrepo, et al. Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial. *Lancet* 2015; published online July 31, 2015 [Text] Ebola vaccine chosen for second round of testing in the Guinea efficacy trial (WHO)
Abbreviations: AE, adverse events; SAEs, serious adverse events; EVD, Ebola virus disease			

Table 4. Heterologous Prime-Boost Regimens using MVA-BN®-Filo and Ad26.ZEBOV vaccines (*Johnson & Johnson/Crucell Holland BV*)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[25] *A Phase 1, First-in-Human Study to Evaluate the Safety, Tolerability and Immunogenicity of Heterologous Prime-Boost Regimens Using MVA-BN®-Filo and Ad26.ZEBOV Administered in Different Sequences and Schedules in Healthy Adults* NCT02313077 Crucell Holland BV-sponsored Oxford, UK Started Dec 2014	MVA-BN®-Filo and Ad26.ZEBOV Heterologous prime-boost regimen Phase 1: safety, tolerability and immunogenicity	MVA-BN®-Filo and Ad26.ZEBOV administered in different sequences and schedules • Part 1: randomized, observer-blind • Part 2: open-label, uncontrolled, non-randomized Enroll 88 adults (ages 18-50 years Immune responses measured by virus neutralization assay and ELISA	Ongoing but not recruiting participants Registry last updated July 23, 2015
[26] *A Phase 1 Study to Evaluate the Safety, Tolerability and Immunogenicity of Heterologous Prime-Boost Regimens Using MVA-BN®-Filo and Ad26.ZEBOV Administered in Different Sequences and Schedules in Healthy Adults* NCT02376400 Crucell Holland BV-sponsored Mwanza, Tanzania, and Entebbe, Uganda Started Mar 2015	MVA-BN®-Filo and Ad26.ZEBOV Heterologous prime-boost regimen Phase 1: safety, tolerability, reactogenicity and immunogenicity	Randomized placebo-controlled, double-blind MVA-BN®-Filo and Ad26.ZEBOV administered in different sequences and schedules Enroll 72 adults (ages 18-50 years) Immune responses measured by virus neutralization assay and ELISA and ELIspot	Currently recruiting participants Registry last updated: July 2, 2015
[27] *A Phase 1, Randomized, Placebo-Controlled, Observer-Blind Study to Evaluate the Safety, Tolerability and Immunogenicity of Heterologous and Homologous Prime-Boost Regimens Using MVA-BN-Filo® and Ad26.ZEBOV Administered in Different Doses, Sequences and Schedules in Healthy Adult Subjects* NCT02325050 Crucell Holland BV-sponsored Rockville, MD, USA	MVA-BN®-Filo and Ad26.ZEBOV Heterologous and homologous prime-boost regimen Phase 1: safety, tolerability and immunogenicity	Randomized, observer-blind MVA-BN-Filo® and Ad26.ZEBOV administered in different doses (standard and higher), sequences and schedules Enroll 128 healthy adults (ages 18-50 years) Immune responses measured by virus neutralization assay and ELISA and ELIspot	Ongoing but not recruiting participants Registry last updated: June 10, 2015

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
Started Jan 2015			
[28] *A Phase 1 Study to Evaluate the Safety, Tolerability and Immunogenicity of Heterologous Prime-Boost Regimens Using MVA-BN®-Filo and Ad26.ZEBOV Administered in Different Sequences and Schedules in Healthy Adults* NCT02376426 Crucell Holland BV-sponsored Ho, Ghana Started Mar 2015	MVA-BN®-Filo and Ad26.ZEBOV Heterologous prime-boost regimen Phase 1: safety, tolerability and immunogenicity	Randomized, placebo-controlled, double-blind MVA-BN-Filo® and Ad26.ZEBOV administered in different sequences and schedules Enroll 72 healthy adults (ages 18-50 years) Immune responses measured by virus neutralization assay and ELISA and ELIspot	Recruiting participants Registry last updated: July 20, 2015
[29] *A Randomized, Observer-Blind, Placebo-Controlled, Phase 2 Study to Evaluate the Safety, Tolerability and Immunogenicity of Three Prime-Boost Regimens of the Candidate Prophylactic Vaccines for Ebola Ad26.ZEBOV and MVA-BN-Filo in Healthy Adults in Europe* NCT02416453 Crucell Holland BV-sponsored France; UK Started June 2015	MVA-BN®-Filo and Ad26.ZEBOV Heterologous prime-boost regimen Phase 2: : safety, tolerability and immunogenicity	Randomized, placebo-controlled, double-blind 3 heterologous prime-boost regimens: all participants receive intramuscular (IM) injection of Ad26.ZEBOV/Placebo on Day 1, followed by IM injection of MVA-BN-Filo or Placebo on Day 29 (group 1), Day 57 (Group 2) and Day 85 (Group 3). Enroll 612 healthy adults (ages 18-65)	Currently recruiting participants Registry updated July 21, 2015
[30] *An Open-label, Controlled Staged Phase 3 Study Using a Cluster Randomization Design to Evaluate the Effectiveness, Immunogenicity and Safety of Ad26.ZEBOV and MVA-BNFilo as Candidate Prophylactic Vaccines for Ebola in an Outbreak Setting EBOVAC – Salone* NCT02509494 PACTR201506001147964 Crucell Holland BV-sponsored Sierra Leone Start July 2015	Ad26.ZEBOV (monovalent and multivalent) and MVA-BNFilo in a heterologous prime-boost regimen Phase 1/2: safety and immunogenicity Phase 3 effectiveness component not yet approved; depends on the course of the epidemic	Open-label, nonrandomized, single group assignment Stage 1: enroll approx. 40 healthy adults (ageds18 years or older) Stage 2: enroll approx. 400 healthy individuals across different age groups, including children (ages 1 year or older) and adolescents.	Not yet recruiting participants Registry last updated July 27, 2015

Table 5. cAd3 and Ad26 Vaccines (*GlaxoSmithKline* and *Johnson & Johnson/Janssen*)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[31] *A Phase I, Safety and Immunogenicity Trial of the Heterologous Prime-boost Regimen Combining the Monovalent Zaire Ebola Viral Vector Candidates ChAd3-EBO-Z and Ad26.ZEBOV in Healthy UK Adults* NCT02495246 University of Oxford-sponsored UK Start July 2015	*ChAd3-EBO-Z and Ad26.ZEBOV* prime-boost regimen Phase 1: safety, tolerability, immune response	Randomized, open-label Enroll 32 healthy adults (ages 18-50) and vaccinate 4 groups with both vaccines one after the other in a prime-boost regimen: • Group 1: ChAd3-EBO-Z, followed by Ad26.ZEBOV 28 days later • Group 2: Ad26.ZEBOV, followed by ChAd3-EBO-Z 28 days later • Group 3:ChAd3-EBO-Z, followed by Ad26.ZEBOV 56 days later • Group 4: Ad26.ZEBOV, followed by ChAd3-EBO-Z 56 days later	Currently recruiting participants Registry last updated Aug 4, 2015
Abbreviations: AE, adverse events; SAEs, serious adverse events; EVD, Ebola virus disease			

Table 6. Recombinant Human Type 5 Adenovirus (Ad5-EBOV) Vector-Based Ebola Vaccine (*Tianjin Cansino Biotechnology*)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[32] *A Phase 1, Dose-escalation, Open Clinical Trial to Evaluate Safety, Tolerability and Immunogenicity of the Recombinant Human Type 5 Adenovirus Vector Based Ebola Vaccine (Ad5-EBOV) in Healthy Adult Africans Aged Between 18-60 Years in China* NCT02401373 First Affiliated Hospital of Zhejiang University-sponsored Hangzhou, Zhejiang, China Started Mar 2015	Ad5-EBOV Phase 1: safety, tolerability and immunogenicity	Nonrandomized, single center, open-label, dose-escalation Enroll 61 healthy adult Africans in China; 30 receive the low dose; and 30 receive high dose (after safety confirmed in low dose group) (ages 18-60 years)	Study completed; no study results posted as of 8/8/15 Registry last updated July 15, 2015
[33] *A Phase 1 Double-blind, Dose-escalation, Clinical Trial to Evaluate the Safety, Tolerability and Immunogenicity of the Ebola Adenovirus Vector Vaccine (Ad5-EBOV) in Healthy Adults in China* NCT02326194 Jiangsu Province Centers for Disease Control and Prevention-sponsored Taizhou, Jiangsu, China Started Dec 2014	Ad5-EBOV Phase 1: safety, tolerability and immunogenicity	Single center, double-blind, placebo-controlled, dose-escalation Enroll 120 healthy adults (ages 18-60 years) Antibody and T-cell responses will be assessed; anti-adenovirus neutralizing antibody responses to the Ebola Zaire vaccine also will be assessed	Ongoing but not recruiting participants Registry last updated March 30, 2015 Zhu FC et al., Safety and immunogenicity of a novel recombinant adenovirus type-5 vector-based Ebola vaccine in healthy adults in China: preliminary report of a randomised, double-blind, placebo-controlled, phase 1 trial. *Lancet* 2015 Mar 24. pii: S0140-6736(15)60553-0 [Text]

Table 7. Glycoprotein (GP) Nanoparticle Vaccine (*Novavax*)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[34] *A Phase 1, Randomized, Observer-Blinded, Dose-Ranging Study to Evaluate the Immunogenicity and Safety of an Ebola Virus (EBOV) Glycoprotein (GP) Nanoparticle Vaccine, With or Without Matrix-M™ Adjuvant, in Healthy Subjects ≥18 to <50 Years of Age* NCT02370589 Novavax-sponsored Queensland, Victoria, and Western Australia, Australia Started Feb 2015	Two doses at a 21-day interval of EBOV GP and Matrix-M adjuvant Phase 1: safety (AEs, SAEs), immunogenicity	Randomized, observer-blinded, placebo-controlled, dose-ranging Enroll 230 healthy adults into 13 different treatment groups (ages 18 to 49 years) Immunogenicity will be assessed by: (1) serum IgG antibody levels as detected by ELISA, (2) epitope-specific immune responses to the EBOV GP antigen, and (3) serum EBOV neutralizing antibody reciprocal titers as detected by a VSV pseudotype-based method	Ongoing but not recruiting participants (Last verified on ClinicalTrials.gov Mar 2015)
Abbreviations: AE, adverse events; SAEs, serious adverse events			

Table 8. DNA Vaccines INO-4212, INO-4201, INO-4202, and INO-9012 *(Inovio Pharmaceuticals)*

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[35] *Phase 1, Open-Label Study to Evaluate the Safety, Tolerability, and Immunogenicity of INO-4212 and Its Components, INO-4201 and INO-4202, Given With or Without INO-9012, Administered IM or ID Followed by Electroporation in Healthy Volunteers* NCT02464670 Inovio Pharmaceuticals-sponsored United States Start May 2015	DNA vaccine INO-4212: coding for both the previous and the current outbreak strain Component DNA vaccine INO-4201: coding for past Ebola Zaire virus outbreak strains Component DNA vaccine INO-4202: coding for the current Ebola virus outbreak strain Phase 1: Safety, tolerability, and immunogenicity	Non-randomized, open-label The study evaluates: • Whether INO-4212 vaccine and its components (INO-4201 and INO-4202) generate protective immunity against Ebola virus Zaire • The relative ability of intramuscular versus intradermal administration of the vaccine to elicit immune responses • Whether co-administration of INO-9012, containing the DNA sequence for interleukin-12 (an immune modulator) can boost the immune response Following administration of vaccine, use of brief electrical pulses (electroporation) to help move more DNA into cells more efficiently. Enroll 75 healthy adult volunteers (ages 18-50)	Currently recruiting participants Registry last updated Jun 3, 2015
Abbreviations: AE, adverse events; SAEs, serious adverse events			