WELLCOME TRUST-CIDRAP EBOLA VACCINE TEAM B

EBOLA VACCINE CLINICAL TRIALS

Situation Update – May 2015

This situation update summarizes the clinical trials that have been 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

We identified a total of 25 clinical trials involving the vaccine candidates listed above. The trials include those that are currently recruiting participants, ongoing but no longer recruiting participants, or about to begin recruiting participants. Information on these trials was obtained from the following sources:

- 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)

This information may not necessarily include all clinical trials being conducted or being planned and also may not reflect up-to-date status. For example, an agreement to initiate a phase 3 trial of the Janssen prime-boost vaccine in Sierra Leone was recently announced,[1] but the trial has not yet been finalized and registered on any of the above-mentioned clinical trial registries so it is not yet listed in this summary. 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 CIDRAP Web site.

KEY FINDINGS

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

  Twenty-two 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 13 countries: Mali (2), Uganda (2), Ghana (1), Kenya (1), Gabon (1), Tanzania (1), United States (6), China (2), Canada (1), Germany (1), Switzerland (2), United Kingdom (2), and Australia (1).

[1] World Health Organization. WHO convenes Meeting for the Assisted Review of the Janssen Ebola Zaire Vaccine Clinical Trials Application by Representatives of Ethics Committee and National Regulatory Authority of Sierra Leone in Accra Ghana, WHO Regional Office for Africa, Apr. 27, 2015 [link]

- *Blood.* Twenty 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; one trial (in Gabon) allows children ≥6 years of age to be eligible, but it is unclear whether that study has actually enrolled any children.

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

  Three clinical trials—two phase 2/3 and one phase 3 – have been initiated in 3 countries in Africa (Liberia, Sierra Leone, and Guinea).
  - *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 may have been suspended in April 2015 due to the low incidence of Ebola virus disease (EVD) in Liberia and recent reports suggest that NIAID is considering its options for moving the trial to additional sites in other West African countries.
  - *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 primarily involving the rVSVΔG-ZEBOV vaccine, although the cAd3-ZEBOV vaccine may also be evaluated, depending on vaccine supply and whether there are sufficient numbers of EVD cases occurring. This ongoing trial uses a ring vaccination strategy around cases of disease. Index cases are randomized such that potentially exposed persons in a ring around the index case are either all vaccinated immediately or vaccination of those in the ring is delayed by 3 weeks. Investigators plan to enroll 21,500 participants. The trial also includes vaccination of a subset of front-line health workers, all of whom receive the vaccine.

- **PUBLISHED REPORTS**

  Five 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.

- **SUMMARY TABLES**

  Information about the 25 identified trials is summarized in the following tables (beginning on page 6):

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

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

  Table 3. ChAd3 and rVSV Vaccines (*GlaxoSmithKline* and *Merck/NewLink Genetics*)

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

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

  Table 6. Glycoprotein (GP) Nanoparticle Vaccine (*Novavax*)

- **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 Ebola virus disease, 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 (*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	Recruiting participants (Last verified on ClinicalTrials.gov Aug 2014) Ledgerwood JE et al. Chimpanzee Adenovirus Vector Ebola Vaccine—Preliminary Report. *New Engl J Med* 2014 Nov 26 [link]
[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 (Last verified on ClinicalTrials.gov Mar 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* NCT02354404 PACTR201412000957310 NIAID-sponsored	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	Recruiting participants (Last verified on ClinicalTrials.gov Feb 2015)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
Kampala, Uganda Started Jan 2015		clinical trial and received the investigational VRC-EBODNA023-00-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 (Last verified on ClinicalTrials.gov Jan 2015) Rampling T et al. A Monovalent Chimpanzee Adenovirus Ebola Vaccine—Preliminary Report. *New Engl J Med* 2015 Jan 28 [link]
[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 (Last verified on ClinicalTrials.gov Jan 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)" in Healthy Adults, 18-65 Years of Age, in Bamako, Mali* NCT02368119	cAd3-EBO bivalent (Zaire plus Sudan) Phase 1b: safety, reactogenicity, immunogenicity	Randomized, double-blind Two dose levels of bivalent vaccine Enroll 40 healthy adults (ages 18-65) Antibody and T-cell responses will be assessed	Not yet open for participant recruitment (Last verified on ClinicalTrials.gov Feb 2015)

STUDY TITLE, ID NUMBER, SPONSOR, STUDY LOCATION	*PRODUCT(S), PHASE, OUTCOME MEASURES*	*DESIGN*	*CURRENT STATUS AND PUBLICATIONS*
University of Maryland-sponsored Bamako, Mali Started Feb 2015			
[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 University of Lausanne Hospitals-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	Ongoing but not recruiting participants (Last verified on ClinicalTrials.gov Mar 2015)

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*
[8] *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]
[9] *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]
[10] *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*
[11] *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	Recruiting participants (Last verified on ClinicalTrials.gov Mar 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]
[12] *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 Apr 20, 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]
[13] *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]
[14] *A Phase 1 Randomized, Single-Center, Double-Blind,*	Single dose rVSVΔG-	Randomized, single-center, double-	Ongoing but not recruiting

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
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	ZEBOV Phase 1: safety (AEs) and immunogenicity	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]	participants (Last verified on ClinicalTrials.gov Feb 2015)
[15] *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	Recruiting participants (Last verified on ClinicalTrials.gov Dec 2014)
[16] *STRIVE (Sierra Leone Trial to Introduce a Vaccine Against Ebola)* *rVSVΔG-ZEBOV] Ebola Prevention Vaccine Evaluation in Sierra Leone* NCT02378753 PACTR201502001037220 CDC-sponsored Freetown, Sierra Leone Started Apr 2015	Single dose of rVSVΔG-ZEBOV at $2x10^7$ plaque forming units Phase 2/3: safety(AEs, reactogenicity), efficacy (prevention of laboratory-confirmed EVD)	Unblinded individually randomized to receive immediate vaccination or deferred vaccination (18-24 weeks after enrollment); single dose Enroll 6000 at-risk persons (HCWs, or surveillance, ambulance, or laboratory personnel; ≥18 years of age)	Recruiting participants (Last verified on ClinicalTrials.gov Apr 2015) CDC press release [link]
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*
[17] *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) and immunogenicity in the first 600 participants Phase 3: safety and efficacy	Randomized, double-blind, placebo-controlled, 3-arm study Enroll 28,170 (ages ≥18 years) • Phase 2: enroll 600 adults • Phase 3: enroll 27,570 adults (if no major safety issues identified in the first 600) ELISA and neutralization antigen-specific assays for antibody will be measured for phase 2 participants	Recruiting participants (Last verified on ClinicalTrials.gov Jan 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 [link]
[18] *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 Apr 20, 2015) WHO information available at: • Ebola vaccine efficacy trial ready to launch in Guinea • Questions and Answers – Ebola Phase III Vaccine Trial in Guinea • First Ebola vaccine to be tested in affected communities one year into outbreak
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/Janssen*)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[19] *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 to be measured by virus neutralization assay and ELISA	Ongoing but not recruiting participants (Last verified on ClinicalTrials.gov Mar 2015)
[20] *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 to be measured by virus neutralization assay and ELISA and ELIspot	Not yet open for participant recruitment (Last verified on ClinicalTrials.gov Apr 2015)
[21] *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 to be measured by virus neutralization	Recruiting participants (Last verified on ClinicalTrials.gov Apr 2015)

STUDY TITLE, ID NUMBER, SPONSOR, STUDY LOCATION	*PRODUCT(S), PHASE, OUTCOME MEASURES*	*DESIGN*	*CURRENT STATUS AND PUBLICATIONS*
Started Jan 2015		assay and ELISA and ELIspot	
[22] *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 to be measured by virus neutralization assay and ELISA and ELIspot	Recruiting participants (Last verified on ClinicalTrials.gov Apr 2015)

Table 5. 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*
[23] *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 60 healthy adult Africans in China; 30 to receive the low dose; and 30 to receive high dose (after safety confirmed in low dose group) (ages 18-60 years)	Recruiting participants (Last verified on ClinicalTrials.gov Apr 2015)
[24] *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 (Last verified on ClinicalTrials.gov Apr 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 [link]

Table 6. Glycoprotein (GP) Nanoparticle Vaccine (*Novavax*)

Study Title, ID Number, Sponsor, Study Location	*Product(s), Phase, Outcome Measures*	*Design*	*Current Status and Publications*
[25] *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			