



Protocol Updates...

● PREVAIL I: Partnership for Research on Ebola Vaccines in Liberia

- * **Protocol:** PREVAIL I is a Phase II randomized, double-blind, placebo-controlled study of the chimpanzee adenovirus 3 (ChAd3-EBO Z) -based vaccine and the vesicular stomatitis virus (VSVΔG-ZEBOV) -based vaccine.
- * **Enrollment:** At their one-year follow-up visits in 2016, participants were given the option of enrolling in an additional four years of follow-up to study the duration of immunogenicity, in accordance with an approved protocol amendment. 1,349 participants (99.6%) consented to continue with the extended follow-up. Extended follow-up visits began in February. To date, 1,113 (82.5%) of the Month 24 visits have been completed, with the rest expected to be completed by the end of May.

● PREVAIL II: A Multicenter, Randomized Safety and Efficacy Study of Putative Investigational Therapeutics in the Treatment of Patients with Known Ebola Infection (Medical Countermeasures Randomized Controlled Trial (MCM RCT) in EBOV)

- * **Protocol:** PREVAIL II was a randomized, controlled adaptive Ebola treatment trial, with frequent interim monitoring, to facilitate the following: dropping of poorly performing arms, introduction of new candidate therapies and modification of current optimized standard-of-care (oSOC). The investigational intervention was ZMapp™
- * **Enrollment:** A total of 72 participants enrolled in the trial in the United States, Liberia (5 enrolled), Sierra Leone, and Guinea. The study closed to enrollment in late January 2016. Study results presented at CROI in February 2016 showed the treatment was well tolerated and suggest it may hold some promise as an Ebola treatment. A paper describing the study results in more detail was published in *The New England Journal of Medicine* in October 2016.

● PREVAIL III: Clinical, Immunologic, & Virologic Follow-up of Survivors of Ebola Virus Disease

- * **Protocol:** PREVAIL III is an observational, natural history cohort study that will follow a cohort of EVD survivors and their close contacts in Liberia for 5 years. The protocol includes eye, neurology, semen and birth-cohort sub-studies.
- * **Enrollment:** Thus far, 3,934 individuals (including 1,126 survivors, 2,716 close contacts and 92 participants in the birth cohort) have been enrolled. Sub-study visits continue for the eye study, neurology, birth cohort and semen collection. Vaginal swab, breast milk collection, and semen collection in seronegative contacts ended in December 2016.

● PREVAIL IV: A Double-blind, Randomized, Two-phase, Placebo-controlled, Phase II Trial of GS-5734 to Assess the Antiviral Activity, Longer-term Clearance of Ebola Virus, and Safety in Male Ebola Survivors with Evidence of Ebola Virus Persistence in Semen

- * **Protocol:** PREVAIL IV is a blinded, randomized, two-phase (treatment and longer-term follow-up), two-arm trial of GS-5734 versus placebo to evaluate the safety, tolerability, antiviral activity, and longer-term clearance of Ebola virus from male survivors with persistent Ebola virus in semen at screening.
- * **Enrollment:** Thus far, 32 participants (target sample size 60-120) have been randomized with no reported Serious Adverse Events (SAEs). Referral programs with the men's semen screening programs at ELWA and the MHP have been initiated to increase recruitment. In addition, mobile units have been deployed to enhance enrollment in the rural counties. Given new information from Gilead Sciences that the active renally excreted metabolites of GS-5734 are not responsible for hepatotoxicity, the team has sought and received concurrence from the FDA on adjusting inclusion criteria and risk mitigation.

• PREVAIL V: Partnership for Research on Ebola VACCination (PREVAC)

- * **Protocol:** PREVAIL V is a randomized, double-blind, placebo-controlled trial of three vaccine strategies to be conducted in multiple sites across 3 countries in West Africa. The three vaccine strategies to be studied are the rVSVΔG-ZEBOV-GP vaccine, with and without a boost at 56 days, and the Ad26.ZEBOV/MVA-BN-Filo vaccine. The study has been initiated with two arms, placebo and Ad vaccines, and the rVSV Ebola vaccine arms will be included in the future.
- * **Enrollment:** The study started in Landréah, Guinea on March 27th, and began a week later on April 3rd in Liberia. The Redemption Hospital site in Liberia has so far enrolled 31 adult participants to date, and there are 48 participants enrolled at the Landréah site. A second site in Maferinyah, Guinea, as well as the Sierra Leone site will initiate in coming months.

• PREVAIL VI: Identification of Host Genetic Factors Underlying Ebola Virus Disease Risk, Mortality, Long-term Sequelae, Viral RNA Persistence, Humoral Immunity, and Ebola Vaccine Response

- * **Protocol:** PREVAIL VI will be a case-control study to identify host genetic factors that underlie the observed variation in disease susceptibility, severity, clinical sequelae, viral persistence, and serological response. We will collect a blood sample, demographics, HIV/syphilis infection status, and medical history from EVD survivors, close contacts of survivors, EVD healthcare workers, and individuals who have received investigational Ebola vaccines (population controls). We will genotype participants and compare results between cohorts to address the study aims. Our results may provide insight into pathogenesis and host immunity and potentially suggest new methods of intervention.
- * **Update:** Protocol is undergoing regulatory review with a planned initiation date by early June 2017.

Recent Publication:



Neurological Complications and Sequelae of Ebola Virus Disease

Bridgette Jeanne Billioux, MD*

Curr Infect Dis Rep (2017) 19:19. DOI 10.1007/s11908-017-0573-x

Purpose of Review: The recent 2014–2016 outbreak of Ebola virus disease (EVD) has led to many discoveries regarding Ebola. Although neurological symptoms during EVD had been previously described, many reports since this outbreak have made clear that EVD can lead to neurological issues. This article reviews the various neurological manifestations of EVD.

Recent Findings: Recently, many neurological symptoms have been described during acute EVD, including altered mental status, seizures, and meningoencephalitis, among others; survivors of EVD also may develop neurological sequelae, such as persistent headache and memory loss, and can exhibit abnormalities on neurological exam. Additionally, it is now evident that in rare cases, survivors may experience relapses of EVD months after recovery, including issues in the central nervous system (CNS).

Summary: EVD can result in many clinical neurological manifestations, both acutely and after recovery. Research is ongoing to further clarify the nature of Ebola in the CNS.

* Dr. Billioux is a neurologist and clinical fellow at the National Institute for Neurology Disorders and Stroke, and supports the PREVAIL III neurology sub-study. A recent protocol amendment has been approved to allow a small set of Liberian participants to travel to the U.S. for a detailed clinical diagnostic examination at the NIH Clinical Center, to include neurological, neuropsychological, imaging, and laboratory testing. These protocol evaluations will hopefully provide important information about the neurological complications and sequelae from Ebola Virus Disease which cannot be determined within the limitations of diagnostics available in Liberia.

Recent Events...

PREVAIL V (PREVAC) Opening Ceremony in Liberia at Redemption Hospital, New Kru Town, on April 2, 2017:



Director General's Message

The Director General of the National Public Health Institute, Hon. Tolbert Nyenswah, has said that his institution will work with PREVAIL and the NIH to achieve their research goals in Liberia.

Hon. Nyenswah discussed how he sees Liberia benefiting from the research partnership and collaboration with NIH.

He said Liberia will do its utmost to uphold ethical research standards.

He used the occasion to recognize PREVAIL's researchers and scientists for their roles in the fight against Ebola.



Ambassador's Message

U.S. Ambassador Christine Elder has praised the collaboration between Liberian and U.S. researchers in an effort to find vaccines and therapeutics to tackle Ebola.

The statement was contained in an address delivered on her behalf by Dr. Emily Kainne Dokubo, Deputy Director for Programs at the U.S. Centers for Disease Control and Prevention.

Amb. Elder commended PREVAIL for being a true partnership from the beginning, with Liberian doctors serving as principal investigators in each of the studies with their U.S. colleagues, in addition to the 300+ Liberian doctors, nurses, and other staff who conduct the studies at PREVAIL's respective sites.

Congratulations to the Prevail V (PREVAC) study team in West Africa on a successful trial initiation!!!

In the news...

NEWS

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

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FOR IMMEDIATE RELEASE

Successful Clinical Trials to Create Drugs and Vaccines for Next Pandemic Disease Will Rely on Building Capacity, Community Engagement, and International Collaboration Before and During Outbreak

WASHINGTON – The rapid mobilization of a robust clinical research program to explore the safety and efficacy of investigational therapeutics and vaccines during the next infectious disease epidemic will depend on strengthening capacity in low-income countries for response and research, engaging people living in affected communities, and conducting safety trials before an epidemic hits, says a [new report](#) from the National Academies of Sciences, Engineering, and Medicine. Using key lessons learned from the Ebola epidemic in West Africa, the report outlines how to improve the speed and effectiveness of clinical trial research while an epidemic is occurring, especially in settings where there is limited health care and research infrastructure.

The study was sponsored by the U.S. Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response, U.S. National Institutes of Health, and U.S. Food and Drug Administration. The PREVAIL team participated in the yearlong U.S. National Academy of Sciences review of Ebola research conducted during the outbreak. After a lengthy review and multiple meetings in Washington, London, and Monrovia, the NAS committee has released the report.

The full PDF report is available at: <http://www.nap.edu/24739>