Corey: Support for HVTN 702

OVERVIEW

HVTN 702 is a pivotal phase 2b/3 multi-site, randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120/MF59 in preventing HIV-1 infection in adults in South Africa. It is co-funded by the NIAID's Division of AIDS (DAIDS), and conducted by the HIV Vaccine Trials Network (HVTN). The trial is designed to provide data that might verify and extend the findings of the modest efficacy and the correlates of risk observed in the RV144 trial conducted with a similar pox/protein HIV vaccine regimen in Thailand. HVTN 702 is a culmination of collaborative efforts by the Pox Protein Public Private Partnership (P5) whose members include BMGF, NIAID, the Fred Hutchinson Cancer Research Center, Sanofi-Pasteur, Glaxo-Smith Kline, and the Medical Research Council of the Republic of South Africa. P5 efforts have included the development of clade C vaccine products adapted to match the circulating HIV clade most prevalent in this region as well as other vaccine regimen modifications designed to enhance the magnitude and durability of immune responses that were found to correlate with a decreased risk of HIV infection risk in RV144. HVTN 100, the antecedent phase 1-2 trial of this vaccine regimen fulfilled specific pre-determined immunogenicity criteria predicated on these immunological correlates from RV144, leading to the decision to proceed with the HVTN 702 trial.

This phase 2b/3 trial of the ALVAC-HIV (vCP2438) / Bivalent Subtype C gp120/MF59 prime-boost vaccine regimen will enroll a total of 5400 healthy, HIV-1–uninfected adults who are aged 18 to 35 years and who are at risk for HIV infection, across 15 research sites in South Africa. Participants will be enrolled over 20–22 months and randomized with equal probability to the placebo or vaccine regimen with n = 2700 in each group. The study is designed to enroll approximately 60% women. Participants will receive ALVAC-HIV (vCP2438) or placebo at months 0, 1, 3, 6, 12 and 18 and will receive Bivalent Subtype C gp120/MF59 or placebo at months 3, 6, 12 and 18. There are 2 co-primary objectives:

- To evaluate the preventive vaccine efficacy (VE) of ALVAC-HIV (vCP2438) + Bivalent Subtype C gp120/MF59 for the prevention of HIV infection in HIV-seronegative South African adults over 24 months from enrollment
- To evaluate the safety and tolerability of ALVAC-HIV (vCP2438) + Bivalent Subtype C gp120/MF59 in adults in South Africa

HIV diagnostic tests will be administered at Month 0 and every 3 months thereafter, with all participants followed to 24 months (Stage 1). Overall, the study design provides approximately 90% power to detect VE from enrollment through 24 months [VE(0-24)] of at least 50% (versus the null hypothesis of H0: VE(0-24) ≤ 25%). If the lower bound of the 95% confidence interval for VE(0-24) is > 0% at the end of Stage 1, all participants will continue follow-up to 36 months (through Stage 2); if Stage 2 occurs, evaluation of the durability of the vaccine efficacy from enrollment through 36 months is included as a secondary objective.

Other secondary objectives include evaluation of: VE from Month 6.5 (Week 26) through 24 months post enrollment; immunogenicity of the vaccine regimen; immunogenicity and immune response biomarkers among vaccine recipients at Month 6.5 as correlates of risk of subsequent HIV acquisition between Month 6.5 and Month 24, with an expanded scope of analysis if Stage 2 occurs; VE by various demographic characteristics; if and how VE depends on genotypic characteristics of HIV, such as signature mutations; genomic sequences of viral isolates from HIV-1– infected vaccine and placebo recipients; and whether there is evidence of vaccine-induced immune pressure on the viral sequences through sieve analysis methods.

The trial will include monitoring by NIAID's independent DSMB for harm, futility/non-efficacy and high efficacy. Early stopping of the vaccine regimen will be recommended if one of the potential harm or non-efficacy boundaries is met at a pre-specified analysis time. Other contingency plans address trial procedures if the high-efficacy boundary is met at a planned interim analysis, and the aforementioned refinement of continuing the trial to Stage 2.

If efficacy is demonstrated at Stage 1 analysis, then this is expected to trigger further product process development and additional activities needed to support an application for market authorization in RSA of an HIV vaccine regimen with an indication to prevent HIV acquisition in adults in South Africa. Additional trials are anticipated in this endeavor as well, the details of which are still under development, but include adolescent trials, evaluation of phase 3 clinical trial material and lot-to-lot consistency trials, among others.

This grant is led by Larry Corey, MD (FHCRC), Glenda Gray, MD (Medical Research Council of South Africa), and Jim Kublin, MD (FHCRC). The HVTN 702 protocol involves engagement of many biomedical research organizations and as well as the 15 South African clinical sites and a multitude of community representatives and in-country partners. The award was made in August 2016, with an original agreement length of 64 months; the BMGF grant is primarily directed to the support of the clinical research sites.

Grant at a Glance

Principal Investigator
Larry Corey, MD

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Grantee Institution
Fred Hutchinson Cancer Research Center, Seattle, WA USA

Project Title
HVTN 702: "A pivotal phase 2b/3 multi-site, randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120/MF59 in preventing HIV-1 infection in adults in South Africa"

OPPID
1148133

Grant Award
Up to $64 million, awarded in August 2016, over an expected duration of 64 months