

Scientific Abstract for 6124K2-1000

The development of a safe and effective therapeutic HIV-1 vaccine is a global health priority. Wyeth is pursuing development of a HIV multiantigen DNA vaccination strategy in combination with *IL-12* DNA, which, as an adjunct to highly active anti-retroviral therapy (HAART) would prolong the effectiveness of therapy. This first-in-man phase 1 trial with the HIV *gag,pol* and HIV *nef,tat,vif,env* DNA vaccine combined with *IL-12* DNA will evaluate safety, tolerability and immunogenicity in healthy HIV-uninfected subjects prior to proceeding to an HIV-1 infected cohort. Vaccination of healthy subjects should provide a clear assessment of the vaccine's ability to induce a cellular immune response, independent of the variability of responses observed in HIV-infected subjects. In addition, results from this trial may determine whether Gag-specific cellular responses, crucial to the control of viremia in HIV infected subjects, will be altered if delivered in combination with the Nef, Tat, Vif and Env expressing DNA plasmid.

The multicenter, randomized, modified double-blind, placebo-controlled trial will involve approximately 35 healthy, HIV-1 uninfected subjects.

In a study in rhesus macaques, a robust cell-mediated immune response to the HIV-1 derived antigens was obtained with the HIV *gag,pol* DNA+ HIV *nef,tat,vif,env* DNA + and *IL-12* DNA vaccine.

The objectives of the present study are:

Safety

To evaluate the safety and tolerability of intramuscular administration of HIV-1 *gag/pol* and the combination of HIV-1 *gag/pol* and *nef/tat/vif/env* DNA vaccine administered with *IL-12* DNA in healthy HIV-1 uninfected subjects.

Immunogenicity

To evaluate the ability of the HIV-1 *gag/pol* and the combination of HIV-1 *gag/pol* and *nef/tat/vif/env* DNA vaccine when administered with *IL-12* DNA to elicit HIV- specific T-cell responses using IFN- γ and *IL-2* ELISpot assays in healthy HIV-1 uninfected subjects.

Exploratory

To evaluate the ability of HIV-1 *gag/pol* and the combination of HIV-1 *gag/pol* and *nef/tat/vif/env* DNA vaccine when administered with *IL-12* DNA to elicit HIV- specific CD4/CD8 T-cell responses measured by ELISpot assay and by using other cellular immune function assays (such as Intracellular Cytokine Staining ICS assay) over the course of vaccination in healthy HIV-1 uninfected subjects. HIV-1 specific antibody responses to the study vaccine antigens may also be evaluated.