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A Novel Therapeutic HIV-1 Vaccine Trial in Patients under HAART

Tung F.[1], Tung J.[1], Pallikkuth S.[2,3], Termini J. M.[4], Gupta S.[2], Babic D.[3,5], Stevenson M.[3,5], Pahwa S.[2,3], Fischl M.[3,5], Stone G. W.[2,3]

[1]GeneCure Biotechnologies, Peachtree Corners, United States, [2]University of Miami, Microbiology and Immunology, Miami, United States, [3]Miami Center for AIDS Research, Miami, United States, [4]University of Miami, Pathology, Miami, United States, [5]University of Miami, Medicine, Miami, United States

Background: HIV-1 specific cellular immunity plays an important role in controlling viral replication. In this first-in-human therapeutic vaccination study, a replication-defective HIV-1 vaccine (HIVAX™) was tested in HIV-1 infected subjects undergoing highly active antiretroviral therapy (HAART) to enhance anti-HIV immunity. The goal of this study is to control viral load and reduce the dependency and side effects of antivirals in HIV patients.

Methods: A010 is a randomized, placebo-controlled dose-escalation trial to evaluate the safety and the immunogenicity of two doses of a replication defective HIV-1 vaccine (HIVAX™) in subjects receiving stable HAART with HIV-1 RNA <50 copies/ml and CD4 cell count >500 cells/mm3. Immunogenicity was measured by interferon-γ ELISPOT and intracytoplasmic cytokine production assay during vaccination. Viral reservoir and immune activation associated with persistent viral infection were also measured during vaccination. Following the randomized placebo-controlled vaccination phase, subjects who received active vaccine and who meet eligibility undergo a 12-week analytical antiretroviral treatment interruption (ATI). Viral loads in plasma were measured by real-time PCR during study. Results of low dose vaccine are reported.

Results: HIVAX™ was well tolerated. Transient grade 1 to 2 (mild to moderate) injection site reactions occurred in 8 of 10 vaccinated participants. HIVAX™ was highly immunogenic in all vaccinated subjects. Proinflammatory cytokines (TNF-α, IL-6, IL-8, IL-1ß, LTA, IL-15), Th1 cytokines (IL-12, IL-2, and IFN-γ), IL-4, LPS, and sCD163 were all significantly reduced in subjects following HIVAX™ vaccination. In contrast, cytokines associated with a Th2/Th17 response (IL-10, IL-5, IL-13, IL-17, and IL-23) did not significantly change following HIVAX™ vaccination. Median viral load (3·45 log10 copies/ml) at the end of 12-week treatment interruption in HIVAX™ vaccinated group was significant lower than two placebo groups of historical data (4·28 log10 and 4·86 log10 copies/ml). Furthermore, three vaccinated subjects extended ATI for up to 2 years and still maintained stable CD4 counts and low viral load.

Conclusions: HIVAX™ vaccine was generally safe, immunogenic and may be effective in controlling viral load during treatment interruption in HIV-1 subjects of trial cohort.