

CYTOTOXIC T LYMPHOCYTE RESPONSES IN PARTICIPANTS ENROLLED IN A PHASE I/II CANARYPOX (ALVAC)/GP 120 B/E PRIME-BOOST HIV VACCINE TRIAL IN THAILAND

de Souza M, Karnasuta C, Cox JH, Nitayaphan S, Pittisituttithum P, Brown AE, Gurunathan S, Heyward W, Birx D and TAVEG

Background: The frequency of cytotoxic T lymphocyte (CTL) responses was determined in HIV-seronegative recipients of canarypox (ALVAC-vCP1521) expressing HIV subtype E Env and B Gag/Pro and HIV recombinant bivalent gp120 (AIDSVAXÒ B/E) as a boost.

Methods: The injection regimen was 0, 1, 3 and 6 months. Five subjects were initially enrolled in an open-label study to assess the safety of ALVAC-vCP1521 (Aventis Pasteur, Lyon, France). Volunteers in phase II were randomly assigned into 3 groups. Group I (N=30) received placebo; Groups II (N=45) and III (N=45) received ALVAC-vCP1521. Groups II and III received a boost of 200µg and 600µg of AIDSVAXÒ B/E (VaxGen, Inc., Brisbane, USA), respectively. CTL assays using chromium release were conducted at 6 time-points from baseline through 6 months following completion of immunisations. Freshly isolated PBMC were stimulated *In vitro* with clade E and B antigens and used as effectors with autologous EBV-transformed B cells infected with recombinant vaccinia viruses expressing clade E Env and clade B Gag/Pol antigens as targets. CD8 specificity of a positive CTL response was assessed.

Results: CTL responses conducted at baseline on 121 volunteers were uniformly negative. The cumulative prevalence of HIV-specific CD8+ CTL activity in the ALVAC group was 24% (22/93). No placebo recipients demonstrated CTL activity. Initial positive CTL responses were observed as early as two weeks following the second injection (3%), and as late as 6 months following the fourth-injection (last time point assessed). The time-point with the greatest CTL activity was 6 months following the last injection (11%). CTL responses were observed to both Env and Gag/Pol antigens. Cross-clade CTL responses to subtype E Gag antigen were observed in 3/8 subjects tested.

Conclusion: ALVAC-vCP1521 induces CTL activity against HIV Env and Gag antigens as early as post-second injection, prior to the protein boost. ALVAC-vCP1521 is capable of inducing cross-clade CTL activity, thus supporting its use as a phase III vaccine candidate in Thailand where two HIV subtypes are circulating.

XIV International AIDS Conference. Barcelona, Spain. 7-12 May 2002.
