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A Phase 1 study to evaluate the safety and immunogenicity of a recombinant HIV type 1 subtype C-modified vaccinia Ankara virus vaccine candidate in Indian volunteers.

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Abstract

A recombinant modified vaccinia Ankara virus vaccine candidate (TBC-M4) expressing HIV-1 subtype C env, gag, tat-rev, and nef-RT genes was tested in a randomized, double-blind, dose escalation Phase I trial in 32 HIV-uninfected healthy volunteers who received three intramuscular injections of TBC-M4 at 0, 1, and 6 months of 5 x 10(7) plaque-forming units (pfu) (low dosage, LD) (n = 12) or 2.5 x 10(8) pfu (high dosage, HD) (n = 12) or placebo (n = 8). Local and systemic reactogenicity was experienced by approximately 67% and 83% of vaccine recipients, respectively. The reactogenicity events were mostly mild in severity. Severe but transient systemic reactogenicity was seen in one volunteer of the HD group. No vaccine-related serious adverse events or events suggesting perimyocarditis were seen. A higher frequency of local reactogenicity events was observed in the HD group. Cumulative HIV-specific IFN-gamma ELISPOT responses were detected in frozen PBMCs from 9/11 (82%), 12/12 (100%), and 1/8 (13%) volunteers after the third injection of the LD, HD, and placebo groups, respectively. Most of the responses were to gag and env proteins (maximum of 430 SFU/10(6) PBMCs) persisting across multiple time points. HIV-specific ELISA antibody responses were detected in 10/11, 12/12, and 0/8 volunteers post-third vaccination, in the LD, HD, and placebo groups, respectively. No neutralizing activity against HIV-1 subtype C isolates was detected. TBC-M4 appears to be generally safe and well-tolerated. The immune response detected was dose dependent, modest in magnitude, and directed mostly to env and gag proteins, suggesting further evaluation of this vaccine in a prime-boost regimen.