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BACKGROUND:

We conducted a double-blind, randomized, placebo-controlled Phase I study of a recombinant replication-defective adenovirus type 5 (rAd5) vector expressing HIV-1 Gag and Pol from subtype B and Env from subtypes A, B and C, given alone or as boost following a DNA plasmid vaccine expressing the same HIV-1 proteins plus Nef, in 114 healthy HIV-uninfected African adults.

METHODOLOGY/PRINCIPAL FINDINGS:

Volunteers were randomized to 4 groups receiving the rAd5 vaccine intramuscularly at dosage levels of 1×10(10) or 1×10(11) particle units (PU) either alone or as boost following 3 injections of the DNA vaccine given at 4 mg/dose intramuscularly by needle-free injection using Biojector® 2000. Safety and immunogenicity were evaluated for 12 months. Both vaccines were well-tolerated. Overall, 62% and 86% of vaccine recipients in the rAd5 alone and DNA prime - rAd5 boost groups, respectively, responded to the HIV-1 proteins by an interferon-gamma (IFN-γ) ELISPOT. The frequency of immune responses was independent of rAd5 dosage levels. The highest frequency of responses after rAd5 alone was detected at 6 weeks; after DNA prime - rAd5 boost, at 6 months (end of study). At baseline, neutralizing antibodies against Ad5 were present in 81% of volunteers; the distribution was similar across the 4 groups. Pre-existing immunity to Ad5 did not appear to have a significant impact on reactogenicity or immune response rates to HIV antigens by IFN-γ ELISPOT. Binding antibodies against Env were detected in up to 100% recipients of DNA prime - rAd5 boost. One volunteer acquired HIV infection after the study ended, two years after receipt of rAd5 alone.

CONCLUSIONS/SIGNIFICANCE:

The HIV-1 rAd5 vaccine, either alone or as a boost following HIV-1 DNA vaccine, was well-tolerated and immunogenic in African adults. DNA priming increased the frequency and magnitude of cellular and humoral immune responses, but there was no effect of rAd5 dosage on immunogenicity endpoints.