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First-in-human phase 1 trial of the safety and immunogenicity of a recombinant adenovirus serotype 5 HVR48 (rAd5HVR48) HIV-1 vaccine

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Background

Adenovirus serotype 5 (Ad5) is a potent vector, but widespread seroprevalence may limit its potential use. Replacement of the hexon variable regions (HVR) of Ad5 with the HVR of the less prevalent Ad48 may result in a potent vector which bypasses pre-existing vector immunity.

Methods

Recombinant Ad5 with seven HVRs derived from Ad48 and expressing the VRC EnvA test antigen (rAd5HVR48. ENVA) was made. 48 healthy volunteers who were seronegative to Ad5, Ad48, HIV-1, and HIV-2 were enrolled in a randomized, double-blind, placebo-controlled, dose-escalation phase 1 study. The first three groups of 12 subjects received doses of 10^9, 10^{10}, or 10^{11} vp of rAd5HVR48.ENVA vector (n=10/group) or placebo (n=2/group) at weeks 0, 4, and 24 and the fourth group received a single injection of 10^{10} vp or placebo. We performed pre-specified blinded immunogenicity analyses at day 56 and day 196 after the first immunization.

Results

31/48 (65%) of subjects were female; median age at enrollment was 24 (range: 18-50). Vaccination was generally well tolerated: mild to moderate local and systemic reactogenicity was observed after the initial immunization, more commonly in the highest dose group, but typically resolved within 24h. No vaccine-associated SAEs occurred. In all four dose groups, 10 subjects per group developed positive EnvA-specific ELISA titers and EnvA-specific interferon-gamma ELISPOT responses following vaccination. Immune responses were seen two weeks following inoculation in the majority of subjects. Two subjects per group exhibited no vector- or insert-specific immune responses at any timepoint and are presumed placebo recipients.

Conclusion

The rAd5HVR48 vector is generally safe and immunogenic in humans at all three doses. Immune responses against EnvA could be detected two weeks following the first inoculation. Ad5HVR48 is a promising new chimeric vector to evaluate novel inserts in further clinical trials.

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