Finding an HIV vaccine remains an elusive proposition. Thus far, there has been a paucity of HIV vaccine trials, and the majority have been unsuccessful with the vaccine showing no efficacy. A successful HIV vaccine can prevent HIV acquisition or slow down progression to AIDS.

HIV vaccine trials thus far in developed countries include the AIDSVAX B/B study and the STEP study (Americas, Caribbean, and Australia). The former study was unsuccessful. The STEP study was stopped in 2007, as it showed an increase in HIV infection for the first 18 months in uncircumcised men who had neutralizing antibodies to adenovirus-5 (Ad5) at baseline. A therapeutic HIV vaccine trial using HIV-immunogen (Remune) also showed the HIV vaccine was non-eficacious. In developing countries, HIV vaccine trials have included the AIDSVAX B/E study, the Phambili study (South Africa) and the RV144 study (Thailand). The Phambili study was halted after the STEP study results were available. Although the STEP study vaccine induced robust T-cell immune responses, it was not efficacious. Immune correlates were not established with these HIV vaccine studies.

The RV144 study using ALVAC-HIV (vCP1521) with AIDSVAX B/E boosting (VAXGen Env protein boost) in Thailand in low-risk heterosexuals showed a modest level of efficacy of the HIV vaccine (31.2%) (95% CI=1-51) after 3.5 years of vaccination but no effect on viral load. The efficacy at 12 months was 60%. The correlates of immune protection had not been yet established. The search for immune correlates secondary to the vaccine used was undertaken from 2010 to present. The case-control study demonstrated that the binding of IgG antibodies to variable region 1 and 2 (V1V2) of HIV-1 envelope proteins correlated inversely with the rate of HIV infection. The binding of plasma IgA antibodies to Env had a direct correlation with the rate of infection. This was hypothesis-generating-in that vaccines developed to induce V1V2 antibodies and lower levels of Env-specific IgA antibodies may have improved efficacy against HIV infection. These IgA antibodies may have mitigated the effects of the protective antibodies. With regards to the results of the RV144 trial, recent advances have included the promise of structural biology for the design of novel envelope antigens. Recent work has also involved determining the structural biology of this V1V2 region.

HVTN 505 tests a combination of two experimental HIV vaccines (VRC vaccine): a DNA vaccine (priming vaccine) and a recombinant adenovirus vaccine (rAd5) (boosting vaccine). The study involves circumcised men who have sex with men, and who are adenovirus seronegative. HVTN 505 is a phase II, randomized, placebo-controlled, double-blind clinical trial, taking place in US cities. The study will (1) examine HIV acquisition (2) test whether the vaccine regimen can reduce viral load (3) provide safety information (4) provide more information on immune correlates (5) examine the interaction between pre-exposure prophylaxis (PrEP) and HIV vaccines.

The STEP study was stopped five years ago and the recent successful work on immune correlates may allow the field to proceed with more certainty. Further steps could include more proof-of-concept trials, adaptive trial designs, and more work on immune correlates. In further preventive trials, it may be more prudent to involve circumcised individuals.

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