Clade C RV144-like vaccine is immunogenic.

Mathematical modelling of the HIV epidemic suggests that the pandemic could be slowed by a vaccine that is 50% efficacious. The RV144 trial is the only trial to achieve a modest efficacy of 31%. However, post-hoc analysis showed a 60.5% efficacy during the first year. This suggests that improving vaccine-induced immune responses could potentially achieve a vaccine efficacy of 50%.

The vaccine regimen in the RV144 trial expressed HIV immunogens from HIV subtype B/E envelope(env) glycoprotein (gp120) molecules. In order to test if the RV144 vaccine regimen would be efficacious in Sub-Saharan Africa, the RV144 vaccine regimen was adapted to include immunogens from HIV-subtype C. In addition to this, the vaccine adjuvant was changed from alum to MF59, with aim of improving vaccine-induced immune responses. Bekker and colleagues conducted the HVTN100 phase 1/2a clinical trial which aimed at determining the safety and immunogenicity of the Subtype C ALVAC-HIV and bivalent subtype C gp120/MF59 HIV-1 vaccine in low-risk, HIV-uninfected adults in South Africa (ClinicalTrials.gov (NCT02404311)).

Overall, the HVTN 100 vaccine regimen was immunogenic and

induced cellular and antibody mediated immune responses that were observed to be associated with lower risk of HIV acquisition in the RV144 trial, warranting the progression of the vaccine to a phase 2b/3 efficacy trial. Analysis of the antibody profiles, showed that the HVTN 100 vaccine regimen induced a lower frequency of IgG antibodies to the env V1V2 region compared with RV144 vaccinees. Additionally, the HVTN 100 vaccine induced greater frequencies of env-specific IgG3 responses, as well higher magnitude of functional and polyfunctional CD4 T cells that expressed various combination of IFN-γ, TNF, IL-2, IL-4 and CD40L than RV144 vaccinees. Finally, in depth multivariate immune profiling demonstrated that the HVTN 100 and RV144 vaccine regimen induced different immunological profiles. Whether these observed differences is due a differences in antigen sub-types or adjuvant, is yet to be determined.

Journal Article: Bekker *et al.,* 2018. Subtype C ALVAC-HIV and bivalent subtype C gp120/MF59 HIV-1 vaccine in low-risk, HIV-uninfected, South African adults: a phase 1/2 trial. Lancet HIV

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