INTRODUCTION

The identification of correlates of protection for preventive HIV vaccines has remained an unresolved question. RV144 was a community-based Phase III efficacy trial conducted in Thailand with Alum-boosted gp120 (envelope)-based vaccine, comparing 2.8 and 10 mcg doses of gp120 [1]. The study was designed to test the hypothesis that HIV-1 vaccine-induced antibodies could block the HIV-1 Env V1-V2 region. This vaccine was composed of Alum-boosted recombinant glycoprotein 120 (gp120) and gp41 HIV-1 subtype A [2].

This trial demonstrated a significant reduction in the incidence of HIV infection in those vaccinated with 2.8 mcg gp120. The study showed that 12 months after vaccination, the efficacy was 31.2% against HIV acquisition at 42 months [1]. Moreover, the efficacy varied by vaccine dose, with a lower efficacy of 20.6% at 12 months [2]. The results of this study have generated several hypotheses and additional analyses.

SUMMARY OF IMMUNE CORRELATES OF RISK/PROTECTION

Several key findings emerged from a study of the RV144 correlates of risk:

- IgM antibodies that bind to neutralizing V1-V2 memory protein are correlated with infection risk.
- Low binding plasma IgM correlated with delayed infection risk.
- Higher titers of V1-V2 binding IgG correlated with increased risk of infection.
- Lower V1-V2 binding IgG correlated with increased risk of infection.
- The role of V1-V2 specific immunity in vaccine efficacy was supported by the lower risk of infection at 12 months.
- Anti-gp120 antibodies of vaccine recipients were most likely to bind to the virus.
- Vaccine-induced antibodies targeted a critical residue in V2 (K169), thus providing evidence of a virus sieve effect at this gp120 region in HIV-infected individuals.
- The CRF01-AE had received gp120 protein boosts derived from both subtypes B and C.
- Cross-reactivity to V2 loop peptides of several HIV-1 subtypes (M consensus, A, B, C, D, CRF01, and CRF02). Peptide positions for each sample and analyzed for differences between infected and vaccine recipients.
- The ratio of IgA/IgG HIV-1 specific Env binding was calculated for each sample.
- The odds ratio and p-values for the risk of infection for Env IgG and Env IgA were measured (compared to Env IgA alone); although the p-value was decreased vaccine efficacy.
- Whether V2 antibodies elicited by various envelope immunogens are generalized.
- Whether V2 antibodies might block the gp120-env interaction.
- Whether the induction of IgA blocking ADCC is a potential ‘spine on the wall’.

CONCLUSIONS

- Several of the above results support the hypothesis that V2-specific immunity could be a correlate of protection.
- The anti-gp120 antibodies of vaccine recipients were most likely to bind to the virus.
- Vaccine-induced antibodies targeted a critical residue in V2 (K169), thus providing evidence of a virus sieve effect at this gp120 region in HIV-infected individuals.
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- Whether V2 antibodies elicited by various envelope immunogens are generalized.
- Whether V2 antibodies might block the gp120-env interaction.
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UNANSWERED QUESTIONS

- Whether the antibodies against the gp120-induced ADCC and the antibody against the V1-V2 region are protective.
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REFERENCES