AIDS VACCINE SCIENCE FOR BUSY ADVOCATES

Building on RV144

The RV144 Essentials

RV144 was the first AIDS vaccine trial to show protection against HIV in humans. The prime-boost combination reduced HIV risk by an estimated 31.2 percent over three years of follow-up.

The field moved quickly and collaboratively to identify a set of tests to perform on available samples to identify correlates of risk. This effort yielded two correlates that are clues for future vaccine design.

The experience with RV144 is a powerful reminder of why human clinical trials of vaccines are essential to the search. The field has learned things it could not have predicted and pursued these results with new research and trials.

Modeling shows that a product like RV144 would make a significant impact in many settings in the context of scaled-up combination prevention. It is important to continue to invest energy, financial resources and time in the RV144 follow on agenda.

Glossary

Adaptive design: A trial in which the protocol predefines ways in which the trial can change on an ongoing basis (e.g., study questions, product, number of trial arms), with decisions guided by review of the available data by the trial team.

Assay: A laboratory procedure or test.

Binding antibody: An immune response that attaches to but does not completely inhibit (neutralize) the activity of a pathogen, like HIV.

Correlates of risk: An immune response that predicts whether those who receive the vaccine become HIV-1 infected. It may be causally related to protection or only a marker for the real immune factor(s) that caused protection.

Re-boost: Providing another dose of a previously-administered vaccine regimen.

V1/V2 region: A region on the envelope (outer coat) of HIV that is involved in viral entry into cells

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RV144 (Thai Prime-Boost Trial)
Building on a breakthrough

RV144, also known as the Thai Prime-Boost trial, evaluated a poxvirus vector plus protein vaccine combination, which found evidence of modest protection. At the end of the trial, efficacy was 31.2 percent overall; efficacy at 12 months after immunization was higher.

Within nine months, an international initiative was underway to select the **assays** used to analyze RV144 samples for **correlates of risk**.

Correlates analysis identified one immune response (**binding antibody** to the **V1/V2 region** of HIV envelope) associated with vaccine-induced protection. High levels of the immune substance known as IgA, were associated with decreased protection. Analysis of immune responses is ongoing.

Scientists are seeking to improve on RV144:

- They are following up on questions raised by the correlates analysis: Is the binding antibody to V1/V2 responsible for, or just a sign of protection? What's the structure of the V1/V2 binding site?
- The Pox-Protein Public Private Partnership (P5) has developed regimens for testing in follow-on trials to RV144 in Southern Africa and Thailand. These regimens will be matched to the regions where they are tested, and will contain new components designed to boost and prolong protection.
- A clinical trial to re-boost some of the volunteers in the RV144 trial to see if immune responses can be improved and sustained reported early data showing that the magnitude of immune responses increases, but duration is still an issue.

Planned follow-on trials include: (1) a South African efficacy trial of a regimen developed by the P5; (2) a South African "discovery" trial with an **adaptive design** to gather information on multiple vaccine candidates; and (3) an efficacy trial among Thai MSM using a regimen developed by the P5.

KEY QUESTION
Is an AIDS vaccine possible?

2009-2010

KEY QUESTION
What might explain the RV144 regimen's protection against HIV?

2011-2013

KEY QUESTION
Can we do better?

2014...