HVTN 702: A pivotal phase 2b/3 multi-site, randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of ALVAC-HIV (vCP2438) and Bivalent Subtype C gp120/MF59 in preventing HIV-1 infection in adults in South Africa

Glenda Gray (Chair)
Linda-Gail Bekker (Co-chair)
Kathy Mngadi (PI for CAPRISA Durban ECRS)
WHO ARE WE?
Who is the HVTN?

The HVTN is an international collaboration of scientists, clinical trial sites, and community representatives working with governments and industry in the global search for an HIV vaccine with a goal of speeding the development and testing of HIV vaccine candidates.
We need a vaccine.
...to conquer global and local HIV epidemics.

Globally-
- 35 million people are living with HIV/AIDS
- About 7,000 new infections take place each day

Locally- South Africa (as of 2013)
- There are more than 6 million people living with HIV/AIDS
- About 20% of adults aged 15-49 are living with HIV
Disproportionate burden of HIV in young women in South Africa

HIV infection and tuberculosis in South Africa: an urgent need to escalate the public health response

THE LANCET

Salem S Aboodol Karim, Gavin J Churchyard, Quanraisha Aboodol Karim, Stephen D Lawn

![Graph showing HIV prevalence by age and gender in South Africa and other countries like Kenya, Cameroon, and Malawi.]
Potential Impact of a Vaccine

New Adult Infections in Low- and Middle-Income Countries by Year and Vaccine Scenario

Even a vaccine with low efficacy and limited coverage can impact the epidemic and play a role in preventing future infections

First Signal of Efficacy in an HIV Vaccine Clinical Trial

Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand

S Rerks-Ngarm, JH Kim et al. for the MOPH–TAEG Investigators
RV144 ALVAC Prime, AIDSVAX B/E Trial
31.2% Estimated Vaccine Efficacy

C. Modified Intention-to-Treat Analysis*

Probability of HIV Infection (%)

Years

Vaccine
Placebo
Hypothesis: IgG Antibodies to V1/V2 Can Protect Against HIV-1 Infection
Hypothesis: Monomeric IgA Can Block IgG Binding to HIV-1 Env on Infected Cells and Prevent IgG Protective Functions
Advancing the findings of RV144 in a clade C region of the world (P5 partnership)

Prime: ALVAC vCP1521
Boost: ALVAC vCP1521 plus VAXGEN env protein (B/E)
Schedule: 0, 1, 3, 6 months; 16,000 volunteers; 1:1 vaccine: placebo; follow-up for 3 years

Although protective efficacy was 31.2% at the primary analysis, 42 months after first vaccination, the highest efficacy was observed at 6-12 months.
Pox-Protein Public-Private Partnership (P5)

P5 is a partnership among Bill & Melinda Gates Foundation, HIV Vaccine Trials Network, NIAID, South African MRC, Novartis, Sanofi Pasteur, and U.S. Military HIV Research Program.

Purpose:
To build on the RV144 result and develop and ultimately license HIV pox-protein vaccines with the potential for broad and timely public health impact.

1. Continue to build public-private partnerships critical for success.
2. Work with host countries to support a flexible regulatory strategy in target populations and regions.
3. Generate and incorporate knowledge from the assessment of next-generation vaccine concepts.
Goals: next generation of HIV vaccines

Same if not better prevention of HIV infection in South Africa compared to the RV144

- Correlates of risk consistent across both populations and epidemics
  ......?

- Better and longer lasting protection –?
The Strategy for the ALVAC/Protein Phase 3 Program

Construction of Bivalent Subtype C gp120/MF59

Construction of ALVAC-HIV-C (vCP2438)

Booster at 12 months

Optimize regimen by increasing potency and durability
HVTN 100: Phase 1-2 Trial

First clinical test of the new products (HIV –ve, low risk individuals)

n=252
  • Ensure products are safe
  • Ensure products illicit an immune response

HVTN 702: Phase 2b – 3 Trial

n= 5400 (HIV –ve, high risk individuals)
  • Focus on efficacy
  • Extended safety
  • Licensure
Strategy for the Phase 3 Program

- **HVTN 097**: Designed to evaluate RV144 vaccine regimen in RSA and compare immunogenicity to that in Thailand.
- **HVTN 100**: A standard phase 1 trial of clade C products to decide whether to proceed to phase 3.
- **HVTN 702**: A classic phase 3 RCT assessing efficacy and safety aimed at licensure.
**Study Schema: HVTN 100/702**

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<th>Primary Vaccine Regimen</th>
<th>Booster</th>
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<tr>
<td>Month 0</td>
<td>Month 12</td>
</tr>
<tr>
<td>Month 0</td>
<td>Month 12</td>
</tr>
<tr>
<td>Month 3</td>
<td>Month 12</td>
</tr>
<tr>
<td>Month 6</td>
<td>Month 12</td>
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</tbody>
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<table>
<thead>
<tr>
<th>N (total 252)</th>
<th>ALVAC-HIV (vCP2438)</th>
<th>ALVAC-HIV (vCP2438)</th>
<th>ALVAC-HIV+ Bivalent Subtype C gp120/MF59®</th>
<th>ALVAC-HIV+ Bivalent Subtype C gp120/MF59®</th>
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<td>ALVAC-HIV (vCP2438)</td>
<td>ALVAC-HIV (vCP2438)</td>
<td>ALVAC-HIV+ Bivalent Subtype C gp120/MF59®</td>
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<td>Placebo</td>
<td>Placebo + Placebo</td>
<td>Placebo + Placebo</td>
<td>Placebo + Placebo</td>
</tr>
</tbody>
</table>

**Products:**
- **ALVAC-HIV (vCP2438)** expressing HIV-1 env (clade C gp120), clade B (gp41), gag (clade B) & protease (clade B) (Dose: >1 X 10^6 CCID\textsubscript{50})
- **Bivalent subtype C gp120/MF59 containing 100mcg TV1.Cgp120 & 100mcg 1086.Cgp120**
Community Engagement

Figure 2. Layers of Biomedical HIV Prevention Trial Stakeholders

Global Stakeholders
National Stakeholders
Broader Stakeholders
Community Stakeholders

Examples:
- CEQs, participant’s family, friends, schools, colleagues, peers, local health service providers, traditional leaders, community advisory boards, medical professionals, local policymakers, local media, NGOs, religious institutions, regulatory bodies, ethical review committees, international organisations, international foundations, funders, sponsors, trial sponsors and networks, WHO/UNAIDS

Trial Participant

Various stakeholders may influence or be affected by a biomedical HIV prevention trial. Stakeholders include trial participants and other community stakeholders as well as a broader range of national and international stakeholders.

From UNAIDS/AVAC Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials
Timeline for Phase 3 Program

HVTN 100 Phase 1-2  n=252
ALVAC+bivalent gp120/MF59

HVTN 702 Phase 3  n=5,400
ALVAC+bivalent gp120/MF59

Decision to move to Phase 3

Checkpoint @ 24 Months
HIV VACCINES THE WORLD’S BEST HOPE TO END AIDS

Questions??

HIV VACCINE
TRIALS NETWORK