ALVAC®-HIV and AIDSVAX® B/E Prime-Boost HIV-1 Preventive Vaccine Regimen

Results of the Thai HIV Vaccine Trial, RV144


for the MOPH-TAVEG Collaboration

Primary data were published online by the New England Journal of Medicine 20 October 2009 at 1001 CET.

RV 144

- Trial Objectives and Design
- Demographics
- Results
  - Efficacy
  - immunogenicity
Trial Objectives

Primary

- To determine whether immunization with ALVAC®-HIV (vCP1521) boosted by AIDSVAX® B/E gp120 B/E protects Thai volunteers from HIV infection.
  - 90.8% power to detect difference if true VE=50%
- To determine effect of immunization on viral load after intercurrent infection.
  - 80% power to detect a 0.39 log difference in VL setpoint (if VE = 50%)
  - Mean of log viral load at first 3 planned assessments at/after serologic diagnosis

Secondary

- To determine effect of immunization on CD4 cell count after intercurrent infection.
- To confirm the safety of this vaccine combination.
- To evaluate whether participation is associated with behavior change increasing risk of HIV infection.

Study Vaccines

ALVAC®-HIV (vCP1521)

- Recombinant canarypox vector vaccine genetically engineered to express HIV-1 gp120 (subtype E: 92TH023) linked to the transmembrane anchoring portion of gp41 (subtype B: LAI), and HIV-1 gag and protease (subtype B: LAI).

AIDSVAX® B/E

- Bivalent HIV gp120 envelope glycoprotein vaccine containing a subtype E envelope from the HIV-1 strain CM244 and a subtype B envelope from the HIV-1 strain MN.
Design

- Community-based, randomized, double-blind, placebo-controlled trial (vaccine: placebo 1:1)
- Volunteers: HIV negative, 18-30 years of age
- Excluded: chronic disease, pregnancy or breastfeeding
- 6-month period of study vaccinations
- HIV testing every 6 months for 3 years post-vaccination

Vaccination and Follow-up Schedule

HIV test, risk assessment and counseling

6-month vaccination schedule

3 years of follow-up (every 6 mo.)

ALVAC^HIV (vCP1521) priming at week 0, 4, 12, 24

AIDSVAX^B/E gp120 boosting at week 12, 24
RV 144

- Trial Objectives and Design
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Trial Numbers/Demographics

- 26,676 18-30 yr old screened
  - 40% Female
- 16,402 enrolled
- 16,395 in modified ITT (mITT) analysis
  - 7 were HIV infected at time of first immunization; they are included in safety analysis but not mITT
  - 8197 Vaccine (V): 8198 Placebo (P)
- Baseline Demographics
  - Study arms balanced for gender, age, province and site, marriage status, behavioral risks including drug use, etc.
  - Behavioral Risks: 48% low, 28% intermediate, 24% high
RV 144

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Acquisition – Modified ITT*

- 125 Infections
  - 51 vaccinees
  - 74 placebos
- VE = 31.2% (p = 0.039, two-tailed; OBF adjusted 95% CI 1.1%–52.1%)
  - VE in males (26%) and females (39%)
- Incidence
  - 0.28% HIV incidence in placebo arm; study design based on 0.34% or 78 placebo infections
  - Similar in males and females
- Analysis adjusting for covariates and in a multivariate model showed no impact on VE
Acquisition Endpoint: Modified Intent-to-Treat (mITT)

Vaccine infections: 51
Placebo infections: 74
p = 0.04
Efficacy: 31.2%
95% CI (OBF): 1.1, 51.2

Probability of HIV-1 Infection (%)

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
YEARS

0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5

Placebo
Vaccine

Co-primary Endpoint 2:
No difference in post-infection setpoint viral load

Mean Setpoint Viral Load
Vaccine recipients: 4.3 log_{10}
Placebo recipients: 4.2 log_{10}
p = NS
No difference in post-infection CD4+ T cell count

Mean CD4 T cell count @ notification and verification visits
Vaccine: 554.7/ul (SE = 38.0)
Placebo: 567.5/ul (SE = 27.2)
p = NS

Safety and Reactogenicity

The vaccine regimen was safe and well tolerated.
Trial Objectives and Design
Demographics
Results
- Efficacy
- Immunogenicity
### IFN-γ/IL-2 ICS

**6 months post-final vaccination**

<table>
<thead>
<tr>
<th>Antigen</th>
<th>CD4 V</th>
<th>CD4 P</th>
<th>CD8 V</th>
<th>CD8 P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Env Only</td>
<td>45/142 (32)*</td>
<td>1/54 (2)</td>
<td>5/133 (4)</td>
<td>4/52 (8)</td>
</tr>
<tr>
<td>Gag Only</td>
<td>0/144</td>
<td>0/56</td>
<td>3/136 (2)</td>
<td>1/53 (2)</td>
</tr>
<tr>
<td>Env + Gag</td>
<td>2/142 (1)</td>
<td>0/54</td>
<td>0/131</td>
<td>0/51</td>
</tr>
<tr>
<td>Any HIV</td>
<td>47/142 (33)*</td>
<td>1/54 (2)</td>
<td>8/131 (6)</td>
<td>5/51 (10)</td>
</tr>
</tbody>
</table>

*P <0.0001 compared to placebo

### Ag-Specific Lymphoproliferation

**2 weeks post-final vaccination**

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Vaccinee</th>
<th>Placebo</th>
</tr>
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<tbody>
<tr>
<td>gp120 E (A244)</td>
<td>61/68 (90)</td>
<td>4/24 (17)</td>
</tr>
<tr>
<td>gp 120 B (MN)</td>
<td>51/57 (89)</td>
<td>4/21 (19)</td>
</tr>
<tr>
<td>p24</td>
<td>31/56 (55)</td>
<td>3/22 (14)</td>
</tr>
</tbody>
</table>

P<0.001 compared to placebo group - all Antigens
### Binding Antibody

2 weeks post-final vaccination

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Frequency (%)</th>
<th>Reciprocal GMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>B gp120</td>
<td>140/142 (99)</td>
<td>31207 (800-204800)</td>
</tr>
<tr>
<td>E gp120</td>
<td>14558 (200-204800)</td>
<td></td>
</tr>
<tr>
<td>B p24</td>
<td>74/142 (52)</td>
<td>138 (50-1600)</td>
</tr>
</tbody>
</table>

P<0.0001 compared to placebo group - all Antigens

### Phase I/II versus RV144

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<tr>
<td></td>
<td>B</td>
<td>E</td>
</tr>
<tr>
<td>ELSpot</td>
<td>17%</td>
<td></td>
</tr>
<tr>
<td>CD8 CrCTL</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>LPA</td>
<td>53%</td>
<td>51%</td>
</tr>
<tr>
<td>P24 EIA</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Gp120 EIA</td>
<td>100%</td>
<td>96%</td>
</tr>
</tbody>
</table>
Conclusions

1. The observed vaccine efficacy in the mITT analysis was 31.2% [p = 0.04, 95% CI (OBF) 1.1, 52.1].
2. There is no difference in early viremia between vaccine and placebo recipients.
3. The vaccine regimen is safe and well tolerated.
4. Self-reported behavioral risk was the same in vaccine and placebo groups.
5. Immunogenicity reveals binding Ab, ADCC (RV 135), and CD4+ T-cell responses

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