HIV: RV 144 prime boost HIV vaccine efficacy study

Nelson L. Michael, M.D., Ph.D
Colonel, Medical Corps, U.S. Army

Director
US Military HIV Research Program (MHRP)
Walter Reed Army Institute of Research

WHO/NIH Workshop: Heterologous Prime Boost Vaccine Research in HIV, Malaria, and TB
Rockville, MD

The views expressed are those of the presenter and should not be construed to represent the positions of the U.S. Army or DoD
Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand

Supachai Rerks-Ngarm, M.D., Punnee Pittisutthithum M.D., D.T.M.H., Sorachai Nitayaphan, M.D., Ph.D., Jaranit Kaewkungwal Ph.D., Joseph Chiu, M.D., Robert Paris, M.D., Nakorn Premsri, M.D., Chawetsan Namwat, M.D., Mark de Souza, Ph.D., Elizabeth Adams, M.D., Michael Benenson, M.D., Sanjay Gurunathan, M.D., Jim Tartaglia, Ph.D., John G. McNeil, M.D., Donald P. Francis, M.D., D.Sc., Donald Stablein, Ph.D., Deborah L. Birx, M.D., Supamit Chunsuttiwat, M.D., Chirasak Khamboonruang, M.D., Prasert Thongcharoenn, M.D., Ph.D., Merlin L. Robb, M.D., Nelson L. Michael, M.D., Ph.D., Prayura Kunasol, M.D., and Jerome H. Kim, M.D., for the MOPH–TAVEG Investigators*
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.
Vaccination and Follow-up Schedule

HIV test, risk assessment and counseling

0.5 1 2 3 (time in years)

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 demonstrated efficacy for HIV acquisition

N=16,395
51 vaccine, 74 placebo HIV infected
Est. VE = 31% 95% CI 1-51% (p=0.04)

Rerks-Ngarm et al. (2009, *NEJM*)
Efficacy at 1 year appeared higher

(Kaplan-Meier-based estimates)

<table>
<thead>
<tr>
<th>month</th>
<th>mITT</th>
<th></th>
<th></th>
<th></th>
<th>PP</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events</td>
<td>16</td>
<td></td>
<td></td>
<td>54%</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events</td>
<td>42</td>
<td></td>
<td></td>
<td>60%</td>
<td>21</td>
<td></td>
<td>68%</td>
</tr>
<tr>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events</td>
<td>67</td>
<td></td>
<td></td>
<td>44%</td>
<td>41</td>
<td></td>
<td>41%</td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events</td>
<td>82</td>
<td></td>
<td></td>
<td>36%</td>
<td>53</td>
<td></td>
<td>27%</td>
</tr>
<tr>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Events</td>
<td>95</td>
<td></td>
<td></td>
<td>36%</td>
<td>62</td>
<td></td>
<td>31%</td>
</tr>
</tbody>
</table>

*Lancet Infectious Diseases, in press*
## Binding Antibody Responses
### 2 and 24 weeks post-final vaccination

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Responders (%)</th>
<th>GMT&lt;sup&gt;-1&lt;/sup&gt;</th>
<th>Responders (%)</th>
<th>GMT&lt;sup&gt;-1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>B gp120</td>
<td>140/142 (99%)</td>
<td>31207 (800-204800)</td>
<td>140/142 (99%)</td>
<td>1758 (200-25600)*</td>
</tr>
<tr>
<td>E gp120</td>
<td>140/142 (99%)</td>
<td>14558 (200-204800)</td>
<td>140/142 (99%)</td>
<td>1000 (100-12800)*</td>
</tr>
<tr>
<td>B p24</td>
<td>74/142 (52%)</td>
<td>205 (100-1600)</td>
<td>26/142 (18%)</td>
<td>149 (100-200)*</td>
</tr>
</tbody>
</table>

P<0.0001 compared to placebo group - all Antigens

*: P<0.001 compared to 2 week time-point
What we have learned
What next?
What we have learned—RV 144

- Protection among low incidence heterosexual Thais, VE 31.2% at 42 months
- No effect on post-infection viremia or CD4 count
- Relatively monophyletic circulating variants CRF01_AE
- Efficacy appears to be early and non-durable
- Evoked binding Ab but not measurable, primary isolate Nab— BAb appeared early and decreased by > 10 fold over 6 months
- CD4+ Env responses, but not CD8 responses
- Correlate/surrogate studies.....
What we would want next

- Extend the observation of early 60% efficacy by increasing the durability of such protection (additional boosts)
  - Heterosexual risk groups in Asia
- **Lesson learned:** Ensure that we can elucidate correlates/surrogates of protection with more appropriate sample collection.
- Establish protection in higher incidence populations (additional boosts)
  - Heterosexuals in sub-Saharan Africa
  - MSM in Africa and Asia
RV 144 Correlates Discovery Effort

ADVISORY GROUPS

- Clinical Development
- Product Development Advisory Group
  - Scientific Steering Committee
  - Humoral & Innate Immunity
  - Cellular Immunity
  - Host Genetics
  - Animal Models
  - Scientific Advisory Groups

PA H Steering Committee

MHRP - DAIDS Steering Committee

RV144 Steering Committee

Correlates

Scientific Steering Committee

PA H Steering Committee

MHRP - DAIDS Steering Committee

RV144 Steering Committee

Correlates

Scientific Steering Committee
Case Control Correlates Analysis
Immune-Correlates Analysis of an HIV-1 Vaccine Efficacy Trial

Barton F. Haynes, M.D., Peter B. Gilbert, Ph.D., M. Juliana McElrath, M.D., Ph.D., Susan Zolla-Pazner, Ph.D., Georgia D. Tomaras, Ph.D., S. Munir Alam, Ph.D., David T. Evans, Ph.D., David C. Montefiori, Ph.D., Chitravorn Karnasuta, Ph.D., Ruengpueng Sutthent, M.D., Ph.D., Hua-Xin Liao, M.D., Ph.D., Anthony L. DeVico, Ph.D., George K. Lewis, Ph.D., Constance Williams, B.S., Abraham Pinter, Ph.D., Youyi Fong, Ph.D., Holly Janes, Ph.D., Allan DeCamp, M.S., Yunda Huang, Ph.D., Mangala Rao, Ph.D., Erik Billings, Ph.D., Nicos Karasavvas, Ph.D., Merlin L. Robb, M.D., Viseth Ngauy, M.D., Mark S. de Souza, Ph.D., Robert Paris, M.D., Guido Ferrari, M.D., Robert T. Baile, Ph.D., Kelly A. Soderberg, Ph.D., Charla Andrews, Sc.M., Phillip W. Berman, Ph.D., Nicole Frahm, Ph.D., Stephen C. De Rosa, M.D., Michael D. Alpert, Ph.D., Nicole L. Yates, Ph.D., Xiaoying Shen, Ph.D., Richard A. Koup, M.D., Punnee Pitisuttithum, M.D., D.T.M.H., Jaranit Kaewkungwal, Ph.D., Sorachai Nitayaphan, M.D., Ph.D., Supachai Rerk-Ngarm, M.D., Nelson L. Michael, M.D., Ph.D., and Jerome H. Kim, M.D.
Correlates Case Control Study [1]

- Measured immune responses from:
  - 41 Infected Vaccinees
  - 205 Uninfected Vaccinees
  - 40 Placebo Recipients

- Peak Immunogenicity (2 weeks after final vaccination) - time independent analysis

- Primary Analysis: 6 priority immune response variables / 8 “sensitivity” variables (consider “sensitivity” variables = secondary)

- Secondary Analysis: 29 other immune response variables that passed pilot study criteria for use
Correction for multiple analyses
  - q values < 0.2 (this means any detected correlate can have up to 20% chance of being a false positive)
  - No Bonferroni correction because study is hypothesis generating, and powered for sensitivity.

Definition of each variable established before unblinding – Primary data-set locked prior to analysis

Primary results confirmed by independent statistical team (Emmes)
# Multivariate Logistic Regression: Quantitative Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Relative risk</th>
<th>P-value</th>
<th>Q-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA Binding to Envelope Panel</td>
<td>1.54</td>
<td>0.027</td>
<td>0.08</td>
</tr>
<tr>
<td>IgG Avidity A244 gp120</td>
<td>0.81</td>
<td>0.37</td>
<td>0.56</td>
</tr>
<tr>
<td>ADCC AE.HIV-1 Infected CD4 Cells</td>
<td>0.92</td>
<td>0.68</td>
<td>0.68</td>
</tr>
<tr>
<td>Tier 1 Neutralizing Antibodies</td>
<td>1.37</td>
<td>0.22</td>
<td>0.45</td>
</tr>
<tr>
<td>IgG Binding to gp70-V1V2</td>
<td>0.57</td>
<td>0.015</td>
<td>0.08</td>
</tr>
<tr>
<td>CD4+ T Cell Intracellular Cytokines</td>
<td>1.09</td>
<td>0.61</td>
<td>0.68</td>
</tr>
</tbody>
</table>

All 6 variables together in multivariate analysis, $P=0.08$
Only $\alpha$-Env IgA and IgG gp70:V1V2 binding, $p = 0.009 \ (\log \ reg), 0.012 \ (\text{Cox})$
2 individual variables were significant:
- gp70 V1V2 *inversely* correlates with infection $[q = 0.08]$
  Estimated 43% reduction in infection rate (per SD)
- Plasma IgA *directly* correlates with infection $[q = 0.08]$
  Estimated 54% increase in infection rate (per SD)
V1V2 scaffold IgG and gp120 IgA binding
Scaffolded gp70-V1V2 Protein

V1

V2

HIV-1 V1V2

His$_6$

Scaffold: Murine leukemia Virus gp70

Pinter A, et al.
Vaccine 16:1903, 1998
V1V2-gp70 Scaffold ELISA

Responders = 64%
Cumulative Infection Rates With V1V2-gp70 Scaffold Assay

- Estimated Relative Risk High vs Low = 0.29
Comparison of Infection Rate and Vaccine Efficacy Between Vaccine and Placebo Recipients in the RV144 ALVAC-HIV, AIDSVAX B/E Trial

V1V2 Antibodies

- High V1V2 Antibodies, Increased Vaccine Efficacy
- Low V1V2 Antibodies, Same Infection Rate as Placebos
Plasma IgA Binding To Env Panel (M-B)

Responders: M-B – NA; individual Env 4% (US1) – 92% gp120 CHO GSID
Cumulative Infection Rates With IgA Env Binding Assay

- Estimated Relative Risk High vs Low = 1.89
Comparison of Infection Rate and Vaccine Efficacy Between Vaccinees and Placebo Recipients in the RV144 ALVAC-HIV, AIDSVAX B/E Trial

IgA Magnitude and Breadth Antibodies

High IgA Antibodies, No Efficacy, Same Infection Rate as Placebo—No Enhancement

Low IgA, Increased Vaccine Efficacy
Primary Correlates Summary

- IgG antibodies that bind to scaffolded-V1V2 recombinant protein correlated *inversely* with infection rate.
  - Interactions analysis: no interactions

- Env binding plasma IgA correlated *directly* with infection rate.
  - Interactions: high IgA associated with higher rate of infection, but lower IgA associated with OR < 1 for ADCC, nAb, avidity, ICS

- Caveat: Correlate identification suggests the hypothesis that these may be related to HIV infection rate or to an unknown factor linked to the putative correlate
Secondary Correlates Summary

- 152 secondary variables analyzed
- 2 had q values of less than 0.20.
- IgA antibody binding to group A consensus Env gp140
  - OR positive vs. negative responses = 3.71 (P = 0.001; q = 0.10)
- IgA antibody binding to a gp120 C1 region peptide
  - MQEDVISLWDQSLKPCVKLTPCLCV
  - OR positive vs. negative responses = 3.15 (P = 0.003; q = 0.13)
- This raises the hypothesis that monomeric, plasma IgA responses to C1 could have blocked IgG C1 Ab with ADCC effector activities.
Hypothesis: Monomeric IgA Can Block IgG Binding to HIV-1 Env on Infected Cells and Prevent IgG Effector Function.

CH54 IgG ADCC mediating MAb

CH38 IgA Blocking MAb
Is it V1V2 or both?
Case control analysis of microarray shows trend to inverse correlation at tip of V2 and in CD4 binding site

- Trend of inverse correlation for V2 peptides 54, 55 [starting at positions 166 and 169]
  - Peptide 555 [169-184] = Crown of V2 loop VQKEYALFYKLDVVP
  - Karasavvas et al. describe the vaccine’s V2-crown directed antibody responses
- Trend of inverse correlation for the CD4 binding site peptides 89-90, despite low response rates
  - Among the contact sites for the most potent broadly neutralizing antibodies (e.g., VRC01, VRC03, etc.)
Sieve Analysis of RV144 Breakthrough Viruses supports importance of V2 loop
Sequence variation in position 169

Position 169

MMBootstrap: $p = 0.044$, $q = 0.199$
Gilbert, Wu, Jobes: $p = 0.040$, $q = 0.160$

Model-Based Sieve:
$P(\text{sieve} \mid \text{data}) > 0.9999$, $p = 0.027$, $q = 0.216$

Placebo

Vaccine

Key:
Each subject is represented by a bar.
Bars all have equal height. Insert AA residue, in black, is shown above the midline.
Within a bar, colors depict the fraction of the subject’s sequences with that AA residue.

Edlefsen, SCHARP
Sequence variation in position 181

Position 181

MMBootstrap: p=.039, q = .199
Gilbert, Wu, Jobes: p=0.021, q = .160

Placebo

Vaccine

Key:
Each subject is represented by a bar.
Bars all have equal height. Insert AA residue, in black, is shown above the midline.
Within a bar, colors depict the fraction of the subject’s sequences with that AA residue.

Edlefsen, SCHARP
Summary

- The case control correlates data suggest 2 hypotheses:
  - Binding to gp70:V1V2 correlates inversely with HIV infection rate?
    - A244 and MN V2 crown linear peptides show similar effects
    - Linear epitope microarray data suggest V2 effect
  - Anti-Env IgA M-B correlates directly with HIV infection rate
- Sieve analysis suggests a V2 effect
- Other secondary analyses identify additional potential correlations
  - Cytokine production after stimulation with Env peptides (inverse)
  - IgA binding to C1 ADCC epitopes (direct)
Questions

- Will these correlate of risk generalize to....
  - These products in Thai MSM?
  - ALVAC-gp120 engineered for heterosexuals in Africa?
  - Other HIV vaccines such as DNA/Ad5?
  - **WARNING**—it is textbook (Stan Plotkin’s) knowledge that different vaccines for the same pathogen can have different correlates of risk/protection.

- Is the V2 finding a marker for high Env responders?

- What effector function do binding Ab subserve...mucosal Nab?

- What binding specificities and effector functions do mAb from RV144 vaccine recipients possess?
Moving from correlates of risk to correlate of protection?
V1V2 immune correlate—next steps

- Passive SHIV protection studies in NHP
  - IgG and IgA Env RV 144 Mabs
  - RV 144 high V1V2/low env IgA plasma

- Analysis of levels and qualities of V1V2 responses in past trials

- Analysis of levels and qualities of V1V2 responses in future efficacy trials
New RV144 V2 Human MAbs

- **CH58**: ELRDKKQKVHALFYKLDIVPIED
- **CH59**: ELRDKKQKVHALFYKLDIVPIED

Both CH58, CH59 neutralize Tier 1 AE.92TH023 but not Tier 2 AE.CM244

Both bind to AE. HIV-1 virus infected CD4 T cells

Both mediate ADCC against virus-infected CD4 T cell targets

Mattia Bonisgnori, Kwan-Ki Hwang, Rob Parks, Guido Ferrari, David Montefiori, Georgia Tomaras, Hua-Xin Liao
RV144 V2 Human MAbs

- Bind to V2 region aa 168-183 (C \( \beta \) strand of V1V2)
- CH58- VH5-51, \( V_\kappa \) 6-57
- CH59- VH3-9, \( V_\kappa \) 3-10
- VH mutations 1.8%, 2.8%
- HCDR3 lengths 19,13
PG9, CH01 Broad Neutralizing HIV-1 Antibodies Bind to the Same Env Region as CH58, CH59 RV144

- CH58: ELRDKKQKVHALFYKLDIVPIED
- CH59: ELRDKKQKVHALFYKLDIVPIED
- PG9: ELRDKKQKVHALFYKLDIVPIED
**CH58 epitope**

92TH023: ---VKLTPC[**V1 loop**]LTCNANVTN[**V1 loop**]NVPNIIGNITDEVRNC[**V1 loop**]SNMTTEL[**V1 loop**]DDKKQV[**V1 loop**]HALYKLDIVPI

ZM109: MTTFK[**V1 loop**]LAC[**V1 loop**]CTSTAA[**V1 loop**]HAE[**V1 loop**]AVRHC[**V1 loop**]TNITDD[**V1 loop**]KDDIVPI

CAP45: MTTFK[**V1 loop**]LAC[**V1 loop**]CTSTAAHAEAVRHC[**V1 loop**]TNITDD[**V1 loop**]KDDIVPI

92TH023: EDN---TSS[**V2 loop**]EYRLINC[**V2 loop**]NTS---[**V2 loop**]---VI[**V2 loop**]KQA

ZM109: SSDDASSAASSLYRLISCQT[**V2 loop**]TTEAVDAA[**V2 loop**]TAAK[**V2 loop**]K[**V2 loop**]Y[**V2 loop**]ANDG[**V2 loop**]GEWY[**V2 loop**]Y[**V2 loop**]DDATK[**V2 loop**]TFTV[**V2 loop**]TEGLELVFQ

CAP45: NKNSPSQGNS[**V2 loop**]EYRIC[**V2 loop**]NTS---[**V2 loop**]---VI[**V2 loop**]KQA

**CH59 epitope**

92TH023: ---VKLTPC[**V1 loop**]LTCNANVTN[**V1 loop**]NVPNIIGNITDEVRNC[**V1 loop**]SNMTTEL[**V1 loop**]DDKKQV[**V1 loop**]HALYKLDIVPI

ZM109: MTTFK[**V1 loop**]LAC[**V1 loop**]CTSTAA[**V1 loop**]HAE[**V1 loop**]AVRHC[**V1 loop**]TNITDD[**V1 loop**]KDDIVPI

CAP45: MTTFK[**V1 loop**]LAC[**V1 loop**]CTSTAAHAEAVRHC[**V1 loop**]TNITDD[**V1 loop**]KDDIVPI

92TH023: EDN---TSS[**V2 loop**]EYRLINC[**V2 loop**]NTS---[**V2 loop**]---VI[**V2 loop**]KQA

ZM109: SSDDASSAASSLYRLISCQT[**V2 loop**]TTEAVDAA[**V2 loop**]TAAK[**V2 loop**]K[**V2 loop**]Y[**V2 loop**]ANDG[**V2 loop**]GEWY[**V2 loop**]Y[**V2 loop**]DDATK[**V2 loop**]TFTV[**V2 loop**]TEGLELVFQ

CAP45: NKNSPSQGNS[**V2 loop**]EYRIC[**V2 loop**]NTS---[**V2 loop**]---VI[**V2 loop**]KQA

**PG9 epitope**

92TH023: ---VKLTPC[**V1 loop**]LTCNANVTN[**V1 loop**]NVPNIIGNITDEVRNC[**V1 loop**]SNMTTEL[**V1 loop**]DDKKQV[**V1 loop**]HALYKLDIVPI

ZM109: MTTFK[**V1 loop**]LAC[**V1 loop**]CTSTAA[**V1 loop**]HAE[**V1 loop**]AVRHC[**V1 loop**]TNITDD[**V1 loop**]KDDIVPI

CAP45: MTTFK[**V1 loop**]LAC[**V1 loop**]CTSTAAHAEAVRHC[**V1 loop**]TNITDD[**V1 loop**]KDDIVPI

92TH023: EDN---TSS[**V2 loop**]EYRLINC[**V2 loop**]NTS---[**V2 loop**]---VI[**V2 loop**]KQA

ZM109: SSDDASSAASSLYRLISCQT[**V2 loop**]TTEAVDAA[**V2 loop**]TAAK[**V2 loop**]K[**V2 loop**]Y[**V2 loop**]ANDG[**V2 loop**]GEWY[**V2 loop**]Y[**V2 loop**]DDATK[**V2 loop**]TFTV[**V2 loop**]TEGLELVFQ

CAP45: NKNSPSQGNS[**V2 loop**]EYRIC[**V2 loop**]NTS---[**V2 loop**]---VI[**V2 loop**]KQA

--- also Pro299 (at the V3 base)
RV144 V2 Human Mabs CH58, CH59

- Bind to V2 region aa 168-183 (C β strand of V1V2)
- Footprint at sites of immune pressure (169K)
- Binds to same regions as PG9, CH01
- Cross-blocks PG9, CH01
- CH58, CH59 do NOT bind glycans
- CH01, PG9 DO bind glycans N160, N156
- Peptide/CH58-59 co-crystallization shows binding to α-helix, not β-sheet (McLellan/Kwong)
Planned studies are mutually reinforcing and will amplify public health impact and regional relevance.

**Precedent for vaccine efficacy**

- **RV144**

**Focus on regional public health**

- **THAILAND**
  - High Risk MSM

- **Republic of South Africa (RSA)**
  - High Risk Heterosexual

**Future amplification of global reach**

- **US/EUROPE**
- **SOUTHEAST ASIA**
- **SOUTHERN AFRICA**

**Strategy for achieving potential licensure in target markets and having the broadest public health impact.**
Lessons learned

- **Logistics**: Ensure that we can elucidate correlates/surrogates of protection with appropriate sample collection (type, source, timing, amount).

- **Costs**: Consider restraining real time execution of expensive laboratory studies until a meritorious clinical result is obtained.
  - RV 144 cost $103 million or $6,500 per subject
  - Correlates costs $3 million.

- **Partnerships**. Funders, executors, regulators, normative bodies, industry, community must all work in concert.
  - Sanofi-pasteur for ALVAC
  - GSID for AIDSVAX...next study with Novartis
  - Pox protein public private partnership (NIAID-Gates led)
Collaborators

Duke
Bart Haynes
Larry Liao
Georgia Tomaras
Nathan Vandergrift
Garnett Kelsoe
David Montefiori
Thomas Kepler
Marcella Sarzotti-Kelsoe
Munir Alam

Bill and Melinda Gates Foundation
Nina Russell
Francine McCutchan

HVTN
Peter Gilbert
Nicole Frahm
Julie McElrath

UMDNJ
Abe Pinter

NYU/VA
Susan Zolla-Pazner

Harvard
Joseph Sodroski
Steve Harrison
Norm Letvin

IHV
George Lewis
Tony DeVico

NIH VRC
Gary Nabel
Peter Kwong
John Mascola
Marie Pancera
Jason McLellan

Thai Ministry of Public Health
Acknowledgements

Supported by:
Collaboration for AIDS Vaccine Discovery Grant From the Bill and Melinda Gates Foundation

HVTN, DAIDS, NIAID

With Collaborations with the MHRP and Thai Ministry of Public Health
- National Institute of Allergy and Infectious Diseases (NIAID)
- National Institutes of Health (NIH)
- Division of AIDS (DAIDS)
- U.S. Department of Health and Human Services (HHS)

Center for HIV/AIDS Vaccine Immunology (CHAVI) # U19 AI067854-06