Vaccine-Induced Sero-Positivity/
 Sero-Reactivity (VISP/SR)

Current VISP/R Practices Overview

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VISPR Workshop
March 14, 2013
VISP/SR Workshop Participant Survey

14 questions on VISPR-related practices in HIV vaccine clinical trials
VISP/SR Survey Participants

China CDC
HVTN
IAVI
Harvard
USMHRP
EDCTP
ANRS
UKHVC
VRC

Map showing various countries and regions in different colors, with labels for specific organizations and participants.
Q 1: Protocol Consents

The protocol informed consent describes VISP/R, and associated risks.

9/9 = YES

→ Informed Consent Discussion Group may identify key concepts recommended for inclusion in consents
Q 2: Lab Data

The protocol collects laboratory data on VISP/R.

9/9 = YES*

→ Technical Feasibility, Logistics of Trial
   Follow-up, and Consent Discussion Groups
Q 3: Social Impact Data

The protocol collects data on VISP/R-related social impact events.

5/9 YES

→ Social Impact/Consent Discussion Group may identify recommendations for study conduct
Testing HIV antibody positive due to vaccine

- A participant reported being denied life insurance; investigation revealed denial was due to vaccine-induced positive HIV antibody test.

- A participant with HIV vaccine-induced antibody had a possible occupational exposure to HIV, underwent HIV testing at work, and was initially mis-identified as being HIV-infected.
Q 4: End-of-study HIV Testing

At end of study, vaccine recipients are tested with locally available HIV tests to assess risk of experiencing VISP/R problems within the community.

9/9 = YES

→ Technical Feasibility, Logistics of Trial Follow-up, and Consent Discussion Groups
Q 5: Post-study HIV Testing

Post-study, vaccine recipients are provided with HIV testing at no cost to distinguish VISP/R from true infection for as long as needed.

9/9 = YES

→ Financial Issues of Trial Follow-up discussion group
Q 6: VISP Duration

Post-study, vaccine recipients are offered enrollment in a follow-up protocol to assess duration of VISP/R.

5/9 = YES

→ Logistical Issues of Trial Follow-up Discussion Group
Q7: Study Participant Registry

Research staff maintain records to confirm the identity and treatment assignment of vaccine recipients who may contact the study site in the future for assistance.

9/9 = YES* (longevity unclear)
Q 8: Informing the Field

The clinical research program has presented information about VISP/R publicly, such as at scientific conferences or to health care practitioners or others.

8/9 = YES
July 20, 2010 — Trials of vaccines designed to prevent HIV infection might induce antibodies that will cause false-positive results on routine antibody tests for HIV infection. Although the goal of much vaccine development is to induce the production of protective antibodies, they might also cause a state of vaccine-induced seropositivity/reactivity (VISP), which can confound the interpretation of HIV tests in the absence of HIV infection.
Persistence of vaccine-induced antibodies following HIV-1 DNA prime MVA boost vaccination among healthy Tanzanian volunteers

Background
A phase I/II HIV vaccine trial (HIV023) using a multiclade, multigene HIV-1 DNA prime with two heterologous HIV-1 MVA boosts has been completed among healthy adults in Dar es Salaam, Tanzania.

Study Subjects and Methods

Sixty HIV-uninfected volunteers randomized to three groups of 30 received DNA plasmid expressing HIV-1 gag, pol, env, and nef, 3.3 mg intramuscularly or plasmid at months 0, 1, and 3 using a needle-free injection device (Octomer).

Volunteers were banded into trios with 10 plaque-forming units of recombinant MVA expressing HIV-1 gag, pol, env, or HIV-1 gag only at months 0, 1, and 3, using a needle-free injection device (Octomer).

The volunteers were followed up to 17-22 months after the last heterologous HIV-1 MVA booster was given. The presence of vaccine-induced antibody responses was analyzed.

Diagnostic HIV serological testing was performed using Murex (Abbott, UK) and EIA (Siemens, Germany) for HIV antibodies and HIV-1 IgG antibodies by ELISA and in-house Immunoblot (ABBott, Belgium) assays.

Table 1: HIV-1 response

<table>
<thead>
<tr>
<th>Test</th>
<th>Antibody</th>
<th>Mean OD</th>
<th>Median OD</th>
<th>Long-term follow-up (months)</th>
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</thead>
<tbody>
<tr>
<td>gp120 ELISA</td>
<td>0.000</td>
<td>0.000</td>
<td>Not done</td>
<td></td>
</tr>
<tr>
<td>Ag/mL ELISA</td>
<td>0.000</td>
<td>0.000</td>
<td>2727 (100%)</td>
<td></td>
</tr>
<tr>
<td>Envelope Pluritonal</td>
<td>0.000</td>
<td>0.000</td>
<td>2727 (100%)</td>
<td></td>
</tr>
<tr>
<td>In-house Immunoblot</td>
<td>0.000</td>
<td>0.000</td>
<td>927 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

Negative Social Impact of Preventive HIV Vaccine Clinical Trial Participation: NIAID’s Model of Prevention, Assessment and Intervention

Mary Aliyu, RN, MS and Chen-Yen Lue, MD, MS, MPH
Division of AIDS, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Key Elements of NIAID’s Social Impact Management Model:
1. Developing vaccine volunteers and consent management frameworks.
2. Comprehensive data collection methods and instruments.
3. Developing procedures and tools to improve the consent process.
4. Collaboration with government agencies, NGOs, and industry.
5. Development of categorical analysis of data and the impact of different strategies.

Social Impact Management Protocol:
1. NIAID Social Impact Management Protocol is designed to ensure that the needs of all participants are met.
2. The protocol is structured to provide a comprehensive framework for managing the social impact of vaccine trials.
3. The protocol includes strategies for dealing with potential social issues that may arise during the trial.
4. The protocol is designed to be flexible and adaptable to the specific needs of each trial.
5. The protocol is intended to be used by all researchers involved in vaccine trials.

Conclusion:
- The NIAID Social Impact Management Protocol provides a comprehensive framework for managing the social impact of vaccine trials.
- The protocol is designed to ensure that the needs of all participants are met.
- The protocol is intended to be used by all researchers involved in vaccine trials.
- The protocol is designed to be flexible and adaptable to the specific needs of each trial.
Q 9: Publishing Data

The clinical research program has published clinical data on VISP/R in scientific journals.

\[ \frac{5}{9} = \text{YES*} \]

Others = YES within protocol publications

Manuscripts in development
Informing the Scientific and Medical Community

Interpreting HIV Serodiagnostic Test Results in the 1990s: Social Risks of HIV Vaccine Studies in Uninfected Volunteers

Robert B. Balfe, MD; Mary Lou Clements, MD; Michael C. Keefer, MD; Barney S. Graham, MD, PhD; Lawrence Corey, MD; Richard Spino, PhD; Sue Weissman, MA; Dale Lawrence, MD; and the NIAID AIDS Vaccine Clinical Trials Group

Here’s My Arm

My Personal Experiences Participating in an HIV Vaccine Trial

Mary Ann Hibbert, Inc.

Evaluation of Attitude, Risk Behavior and Expectations among Thai Participants in Phase I/II HIV/AIDS Vaccine Trials

Mary Allen, Heidi Israel, Kyle Rybczyk, Mary Ann Pugliese, Kelley Lough, Lois Wagner, and Shirley Erb

Safety and Immunogenicity of an HIV Envelope Glycoprotein 120 Vaccine in Healthy Thai Adults

Safety and Immunogenicity of Combinations of Recombinant Subtype E and B Human Immunodeficiency Virus Type 1 Envelope Glycoprotein 120 Vaccines in Healthy Thai Adults

BMC Infectious Diseases

Current HIV Vaccines: Impact of HIV Vaccines on Laboratory Diagnostics: Case Series from Thailand

Phaiboon Pattaranarak, MD; Manap Chavanasophon, MD; Phanawan Panyarachun, MD; Phayaw Suwanwela, MD; Chalermin Thawornsiri, MD; Thawawat Thawornsiri, MD; Phuket Hoon, MD; Suprakun Imprakrojanakul, MD; Apasri Pholprasert, MD; and Shireen Ali

Human Immunodeficiency Virus (HIV) Seropositivity among Uninfected HIV Exposed Infants

Trial-Related Discrimination in HIV Vaccine Clinical Trials

Mary Allen, Heidi Israel, Kyle Rybczyk, Mary Ann Pugliese, Kelley Lough, Lois Wagner, and Shirley Erb

BRIEF REPORT

Safety and Immunogenicity of an HIV Envelope Glycoprotein 120 Vaccine in Healthy Thai Adults

MAJOR ARTICLE

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MAJOR ARTICLE
Q 10: Assisting Participants

Research staff provide assistance with VISP/R-related HIV testing in regard to applications for insurance, foreign travel, employment, military service, or other reasons.

9/9 = YES
Q 11: Long-Term Contacts

In the event the protocol clinical site closes, study recipients are provided with a long-term contact for assistance.

7/9 = YES

Comments: “This has not been needed so far”

→ Efficacy trials with multiple protocol-specific trial sites may require up-front planning to address
Q 12: Remote HIV Testing

Participants who relocate can obtain VISP/R-related HIV testing remotely.

5/9 = YES

Comments: YES “in theory”

“not as a rule”
Q 13: Blood Banking

In-country blood banking organizations have been informed about VISP/R.

$5*/9 = YES$
Blood Donation

American Association of Blood Banks
Standards for Blood Donation

Past HIV vaccine trial participation is not exclusionary to blood donation

Thailand Blood Banks

HIV vaccine recipients are ineligible to donate blood.

Placebo recipients with documentation may donate.
Q 14: Other Measures

Participant ID card

HIV Ab tests package inserts address VISP

“A person who has antibodies to HIV-1 is presumed to be infected with the virus except that a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV. Clinical correlation is indicated …”

Voluntary HIV Counseling & Testing Guidelines address VISP

Persons whose test results are HIV-positive and who are identified as vaccine trial participants should be encouraged to contact or return to their trial site or an associated trial site for HIV CTR services.
Insurance Industry

USA
Insurance industry mailings

Republic of South Africa
LOA Code of Conduct:
HIV Testing Protocol
Summary

Q1: Consent 9/9
Q2: VISP data collected 9/9
Q3: Social Impact data 5/9
Q4: EOS testing (local tests) 9/9
Q5: Post-study testing 9/9
Q6: VISP duration data 5/9
Q7: Participant registry 9/9
### Summary cont.

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<thead>
<tr>
<th>Question</th>
<th>Description</th>
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<tbody>
<tr>
<td>Q8</td>
<td>Informing the field about VISP</td>
<td>8/9</td>
</tr>
<tr>
<td>Q9</td>
<td>Publishing data on VISP</td>
<td>5/9</td>
</tr>
<tr>
<td>Q10</td>
<td>Assisting ppts</td>
<td>9/9</td>
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<td>Q11</td>
<td>Long-term contacts</td>
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<td>Q12</td>
<td>Remote HIV testing services</td>
<td>5/9</td>
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<tr>
<td>Q13</td>
<td>Blood banking</td>
<td>5/9</td>
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<tr>
<td>Q14</td>
<td>Other</td>
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<td>HIV ab test package inserts</td>
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<td></td>
<td>VCT guidelines, Insurance industry</td>
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</table>
Current and Future Issues

- **Efficacy trial expansion sites and centralized participant registries**
- **Insurance industry: Life, Health, Disability, Long-Term Care**
  
  *Needed: an industry-accepted HIV testing procedure for vaccine volunteers applying for insurance.*

- **Relocated volunteers**
  
  *Needed: widely accessible blood-draw/shipping services.*

- **Confirmatory HIV testing technology**
  
  Use of rapid antibody testing to **confirm** HIV infection - misdiagnosis of vaccine volunteers? *Needed – rapid NAT*

- **VISP and HIV testing during pregnancy, labor and delivery**
  
  *Needed – improved vaccine volunteer identification and rapid NAT?*

- **VISP and Military service**
  
  *Needed – guidance on informing volunteers re potential impact of VISP on careers in the military.*
The world needs an AIDS vaccine.

You can help find one
Thank you
Danke
Xie xie
Khawp khun
Yum go tic
Salamat
Juspadjaraña
Obrigada
Spacibo
Arigato