
HIV VACCINES AND THE COMMUNITY

The Community Advisory Board Bulletin

Volume 2, Issue 3 March 2001

Scientific Steering Committee- Update from Chicago

By Bill Snow, CAB Representative



Most of you will know that HVTN had two days of meetings after the big annual Retrovirus meeting in Chicago, February 8-9. The two days were largely filled with committee meetings and committee work of the scientific committees, lab sciences, international working group, and various protocol teams. Since it was an opportunity for those present to hear about and discuss the agendas of each group, the Scientific Steering Committee sat in on the other committees and only met independently once, on the first evening.

In that meeting we reviewed the network's progress, discussed discretionary fund proposals, site expansion in preparation for efficacy trials, a conflict of interest policy, partnerships with other vaccine development groups, and the Vaccines 2001 Conference scheduled for September 5-8 in Philadelphia. Let me say a few words about each:

Network Progress: The general consensus is that the network is doing well but that some areas need more attention. Good work in being done by the product development teams and plans are moving forward on scientific agendas for each science committee. Yet the network is not well known yet, there is a great deal of work to be done on many fronts, and things aren't moving as fast as most would like. The greatest accomplishments have been getting the HVTN HIVNET 026 Caribbean and Brazil trial ready to start and the rapid enrollment of HVTN 203 the Phase II ALVAC 1452 trial, which are pivotal to making a decision about moving Canarypox forward. Several other products will be entering Phase I trials, but mostly not until later this year and early next year.

Discretionary Fund: The lab sciences committee has had a number of discretionary fund proposals. The steering committee reconfirmed that committees can approve smaller proposals themselves, but need to do so with the scientific agenda in mind and report back on overall activities and expenditures.

Site Expansion: There was a long and interesting discussion about the balance of identifying and preparing new sites to be ready for efficacy trials before a decision can be made about moving ahead with

the trial. Susan Buchbinder, chair of the Phase III committee believes that work needs to begin now at a number of sites, and that Phase I trials should be conducted at some of them to meet readiness needs for an 11,000 person trial in 2002. The committee agreed in principle, pending a specific plan for each country and site.

Conflict of Interest: This was discussed on the Global CAB call last month. HVTN is developing a policy so that real and perceived financial conflicts of interest can be reviewed and acted upon by the core management of the network, while maintaining individuals' rights to privacy. These will be based on similar policies already in place at most academic institutions where the sites are.

Partnerships: The HVTN is concerned that we work collaboratively with other groups that are doing HIV vaccine development, like the International AIDS Vaccine Initiative and NIH Vaccine Research Center. Representatives of both groups attended the Chicago meeting and talks are going on regarding how we will work together.

September Conference: Announcement have gone out for the Vaccines 2002 Conference, and all network members were encouraged to submit abstracts to the meeting, which will be due in mid May. There will be a category of abstracts for community issues, and a limited scholarship and travel grant program, including international and community scholarships, with preference for presenters. ☘

The VaxGen Community Advisory Board

By Joe Wright, Co-chair of the VaxGen CAB

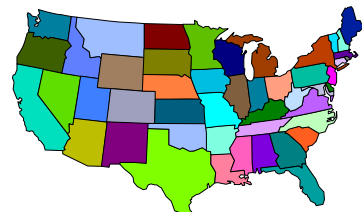
VaxGen is a private company headquartered in the San Francisco Bay Area, which is in the midst of the first phase III efficacy trials of a preventive HIV vaccine. Their vaccine uses two different synthetic versions of gp120, a protein that is on the outside of HIV. VaxGen is conducting two parallel trials: one in Thailand, and another in Puerto Rico, Canada, the Netherlands and the United States, with most of the sites in the US and Canada. For more information about the company, the trial, and the vaccine, go to their website at www.vaxgen.com.

The VaxGen Community Advisory Board (CAB) that advises the US/Canada/Puerto Rico/Netherlands trial is composed both of representa-

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Current HVTN Trial Being Conducted in the U.S.

Hopefully, by now, you all have had a chance to review the the trial concept for the HVTN 203 Protocol, the informed consent documents and other educational materials relating to the trial. If local CABs have not yet reviewed this Protocol, we are hoping that this Bulletin will give everyone a chance to “get up to speed.”



Update from David Lee, the Protocol Specialist for the HVTN 203 Protocol:

As of March 20, 2001, 170 participants have been enrolled in HVTN Protocol 203 by 6 HVTN sites. New site training is almost complete, with 4 new sites coming on board for 203 recruitment (some of the new sites are composed of affiliated sites making the new site total 9). The New York Blood Center at Union Square is the newest site to join for 203 recruitment. ☘

HVTN 203 PROTOCOL SCHEMA

Protocol 203: A Phase II clinical trial to evaluate the immunogenicity and safety of a combined regimen using ALVAC vCP1452 and AIDSVAX™ B/B

Subjects: Subjects at any risk for HIV infection from U.S. HVTN sites

Number of Subjects: 330 Total: 90 control, 240 immunogen

Schema:

A:		ALVAC-HIV vCP1452 approximate dose of $10^{7.26}$ TCID ₅₀				
AP:		PLACEBO – ALVAC at same dose (control for vector)				
B/B:		AIDSVAX™ B/B vaccine (300 mcg/mL MN rgp120/HIV-1 antigen and 300 mcg/mL GNE8 rgp120/HIV-1 antigen in 1.2 mg aluminum hydroxide adjuvant)				
P:		AIDSVAX PLACEBO (aluminum hydroxide adjuvant)				
Group		Number	Immunization Schedule in Months (Days)			
			0 (0)	1 (28)	3 (84)	6 (168)
ALVAC alone	A	120	A + P	A + P	A + P	A + P
ALVAC/ AIDSVAX Combined	B	60	A + P	A + P	A + B/B	A + B/B
	C	60	A + B/B	A + B/B	A + P	A + B/B
Placebo	D	90	AP + P	AP + P	AP + P	AP + P

Product Descriptions: ALVAC-HIV vCP1452 is a recombinant canarypox vector into which the following genes have been inserted: HIV-1 envelope gp120 (strain MN) linked to the transmembrane portion of HIV-1 gp41 (strain LAI), the HIV-1 LAI gene encoding the entire *gag* protein, the sequence of a portion of the *pol* gene encoding the protease, and a synthetic polynucleotide encompassing several known human CTL epitopes from the *nef* and *pol* gene products. It also contains sequences encoding the E3L and K3L vaccinia virus proteins into the C6 site. [Virogenetics Corp., Troy, NY and Aventis Pasteur, S.A., Marcy L'Étoile, France]. AIDSVAX™ B/B is a bivalent recombinant gp120 product based on the MN strain and the primary isolate B clade-derived GNE8 sequence. The antigen is formulated in alum [VaxGen, Brisbane, CA].

Study Duration: 18 months

Monitoring of Trial: DAIDS Vaccine and Prevention Data and Safety Monitoring Board

Sponsoring Agency: Division of AIDS (DAIDS), Vaccine and Prevention Research Program, Vaccine Clinical Research Branch, National Institute of Allergy and Infectious Diseases (NIAID), NIH

Clinical Sites: Columbia University, Harvard University/Brown University, Johns Hopkins University, New York Blood Center, Saint Louis University, San Francisco Department of Public Health, University of Alabama at Birmingham, University of Rochester, Fred Hutchinson Cancer Research Center/University of Washington, University of Maryland at Baltimore, and Vanderbilt University

Study Chair: Barney Graham, M.D., Ph.D., Vanderbilt University

Study Vice-Chair: Michael Keefer, M.D., University of Rochester

Data Coordination: Fred Hutchinson Cancer Research Center

Central Laboratories: Duke University Medical Center, Fred Hutchinson Cancer Research Center/University of Washington, and Viral and Rickettsial Disease Laboratory.

STUDY GOALS

This Phase II trial is directed toward expanding the available data on the safety and immunogenicity of the ALVAC-HIV vector vCP1452 when given alone, and in combination with a gp120 subunit vaccine, AIDSVAX™ B/B gp120 [VaxGen] in a study population that includes volunteers at risk for HIV infection. ALVAC-HIV vCP1452 is a recombinant canarypox vector into which the following genes have been inserted: HIV-1 envelope gp120 (strain MN) linked to the transmembrane portion of HIV-1 gp41 (strain LAI), the HIV-1 LAI genes encoding the entire *gag* protein and the portion of the *pol* sequence sufficient to evoke protease activity. Additional sequences corresponding to CTL epitopes from the *nef* and *pol* genes and sequences encoding E3L and K3L from vaccinia have been inserted to improve

immunogenicity. This vaccine has been tested in healthy immunocompetent adults and has been shown to be well tolerated and immunogenic (Tables 1, 2, and 3).

The primary goal of this vaccine trial is to define the immunogenicity of a single and combined regimen using the best vector-based vaccine with the best purified recombinant envelope protein vaccine identified to date in clinical trials. A secondary goal is to expand testing of this candidate AIDS vaccine regimen into larger numbers of lower risk and higher risk individuals in the U.S. to prepare for the possibility of larger scale trials. The vaccines are to be given to healthy, HIV-1 uninfected adult volunteers. The study will be performed in parallel with HIVNET 026, which will be conducted in Haiti, Trinidad and Tobago, and Brazil.

Primary Objectives:

- To confirm safety of ALVAC-HIV vCP1452 in a study population similar to that proposed for Phase III studies.
- To characterize the safety of ALVAC vCP1452 given in combination with subunit rgp120 formulated in alum.
- To define the frequency of CD8+ CTL responses induced by ALVAC vCP1452 alone or in combination with B/B rgp120.

Secondary Objectives:

- To characterize the optimal combination schedule of rgp120 and ALVAC-HIV vCP1452 with respect to maximal antibody response.
- To directly compare the ⁵¹Cr-release CTL assay with the IFN γ ELISPOT method of measuring vaccine-induced CD8+ T cell response.

INCLUSION CRITERIA

- Age: 18-60 [No more than 10% of the volunteers in each strata to be over age 50]
- Sex: Male or Female [For females, negative pregnancy test at time of entry, unless they have self-reported history of hysterectomy or bilateral tubal ligation, and assurance that adequate birth control measures will be used for one month prior to immunization and for the duration of the study]
- Normal history and physical examination
- Normal complete blood count and differential defined as:
 - Hematocrit $\geq 32\%$ for women; $\geq 38\%$ for men
 - White count $\geq 3,500$ cells/mm³ and $\leq 12,000$ cells/mm³
 - Differential within institutional normal limits or approval of site physician
 - Total lymphocyte count ≥ 800 cells/mm³
 - Absolute CD4 count ≥ 400 cells/mm³
 - Platelets (125,000-550,000/mm³)
- Normal ALT ($\leq 3x$ institutional upper normal limit) and serum Creatinine (≤ 1.6 mg/dl)
- Negative Hepatitis B surface antigen
- Normal urine dipstick with esterase and nitrite
- Negative ELISA for HIV within 8 weeks of immunization
- Availability for follow-up for planned duration of the study (18 months)

SPECIAL INCLUSION CRITERIA for this study:

- For the 340% of volunteers enrolled in the lower risk strata: Lower risk sexual behavior as defined by meeting the criteria for HVTN Risk Group A or B
- For the 340% of volunteers enrolled in the higher risk strata: Higher sexual behavior or injection drug use as defined by meeting the criteria for HVTN Risk Group C or D

EXCLUSION CRITERIA

- History of immunodeficiency, chronic illness, malignancy, autoimmune disease, or use of immunosuppressive medications. Individuals with a history of cancer are excluded unless there has been surgical excision followed by a sufficient observation period to give a reasonable assurance of cure.
- Medical or psychiatric condition or occupational responsibilities that preclude subject compliance with the protocol. Specifically excluded are persons with a history of suicide attempts within 3 years, recent suicidal ideation, or who have past or present requirement for antipsychotic medication.
- Live attenuated vaccines within 60 days of study [NOTE: Medically indicated subunit or killed vaccines (e.g., influenza, pneumococcal) are not exclusionary, but should be given at least 2 weeks away from HIV immunizations.]
- Use of experimental agents within 30 days prior to study
- Receipt of blood products or immunoglobulin in the past 6 months
- Active syphilis [NOTE: If the serology is documented to be a false positive or due to a remote (>6 months) treated infection, the volunteer is eligible.]
- Active tuberculosis [NOTE: Volunteers with a positive PPD and a normal chest X-ray showing no evidence of TB and not requiring INH therapy are eligible.]
- Any history of anaphylaxis or history of other serious adverse reactions to vaccines
- Prior receipt of HIV-1 vaccines or placebo in a previous HIV vaccine trial
- Pregnant or lactating women

SPECIAL EXCLUSION CRITERIA for this study:

- Immediate type hypersensitive reaction to egg products or neomycin (used to prepare ALVAC vaccines)
- History of reaction to thimerosal

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tives of local community advisory boards, and "at-large" national representatives; site staff also sometimes participate. Though VaxGen staff prefer not to know who among us are trial participants, several of our CAB members have "outed" themselves as trial participants either in VaxGen's trial or in other HIV vaccine trials. We meet monthly via conference calls.

An important role of the national CAB is to help facilitate communication between local communities (including trial participants), local CABs, the national CAB and the company. We also help advise VaxGen about ongoing issues like participant retention, which is important to ensure that the trial yields a result. Beyond these core roles, different members of the CAB bring different ideas of what they hope to accomplish by participating. For instance, some see their priority as making sure that the company and the trial sites support participants. Others focus on the impact that the trial may have on the broader community.

These concerns often complement each other. For example, one of our discussion topics for the last few months has been to advise VaxGen about anticipating issues that would accompany the release of data from the trial. Some of us looked at how community HIV prevention agencies and "opinion leaders" might react to data from the trial, and what kind of impact their different reactions might have. Others focused on how participants might feel when data emerges from the trial. We expect that this conversation will lead to more formal recommendations that encompass all of our concerns about how the release of trial results will affect trial participants and the communities to which they belong.

Other CAB business has included advising VaxGen on how to encourage local sites to create structures for community input; advising VaxGen on issues that come up during the trial; and discussing the various substudies that are associated with the VaxGen trial.

One key difference between the VaxGen trial's network of sites and the HVTN network of sites is that there are many more VaxGen sites, each of which has its own particular history and strengths. Some of the VaxGen sites have a long history of CAB involvement, while the idea is new to others. The resulting diversity of CAB approaches, meeting schedules and member backgrounds are brought together in the national CAB.

As with all Community Advisory Boards, it is always a struggle to do everything we would like to do in the midst of all of our other work and obligations; most of us are not paid for the time we spend on CAB business. But we have had many productive discussions, we believe that the company has valued our counsel, and we hope that will continue to be the case.

We have already learned from the connections that some of our individual members have to the HVTN, and we hope that HVTN CAB members and other interested people will feel free to contact us. David Mariner (david@advocatesforyouth.com) and Joe Wright (jmwright@mindspring.com) are the CAB co-chairs, and would welcome correspondence, suggestions, questions and information. ☘

CALENDAR OF EVENTS

CAB PROTOCOL WORKING GROUP CONFERENCE CALL:



Saturday April 7, 2001 12 p.m. EST, 9 a.m. PST. **NOTE NEW DATE**

GLOBAL CAB CONFERENCE CALL:



Thursday April 12, 2001 7 p.m. EST, 4 p.m. PST

COMMUNITY EDUCATION/RECRUITMENT COORDINATION CALL:



Tuesday April 17, 2001 12:00 noon EST, 9:00 a.m. PST

HVTN FULL GROUP MEETING

MAY 9-11, 2001 WASHINGTON D.C.



4TH ANNUAL HIV VACCINE AWARENESS DAY

May 18, 2001



CAB RETREAT, SEATTLE WA

August 16-18, 2001



HVTN Full Group Meeting, May 9-11, 2001

Those persons attending the May HVTN Full Group Meeting should plan to stay on Friday afternoon for the Community Advisory Board session. This will include a combination of committee reports, skills building, planning for the summer retreat, and an update on how other vaccine education processes may affect the HVTN. The meeting will conclude at 5 PM. Please forward agenda items you would like to cover or have covered to the GCAB co-chairs Danny Pickett and Jim Thomas. ☘

Please send suggestion, questions and article submissions to:

Siobhan Malone- Community Project Coordinator

HVTN/FHCRC, 1100 Fairview Avenue North

PO Box 19024, M/S: MW 832

Seattle WA 98109-1024

Siobhan@ssharp.org

Tel: 206-667-6350 Fax: 206-667-6366



HIV VACCINE
TRIALS NETWORK