HVTN 505 Study HIV Vaccine Candidate Not Effective

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The National Institute of Allergy and Infectious Diseases (NIAID) and the HIV Vaccine Trials Network have announced there will be no further vaccinations of participants in the HVTN 505 study because the vaccine did not show efficacy. This means it did not work to prevent HIV infection nor reduce the amount of virus (viral load) in the blood among people in the study who became infected with HIV.

Like every study that tests whether or not an experimental drug or vaccine will work, this study has been closely monitored by a group of experts called a Data Safety Monitoring Board (DSMB). This group of experts regularly reviews study information to make sure that the study remains safe for participants in these studies, and we have heard many stories of the study volunteers giving site staff encouragement when study results are not favorable, rather than vice versa. The people receiving the experimental vaccines who are giving their arms and their blood are consoling the scientists.

Study volunteers make us aware of how inhumane and severe the HIV pandemic really is, and how difficult it is to prevent HIV infections among so many communities. Whether in San Francisco, Nashville, Lima or Johannesburg, the HIV pandemic continues to burn. And it burns despite the great progress the scientific community has made regarding treatment and non-vaccine prevention. This awareness at times is discouraging, but it also inspires us to work harder and more openly to make progress. To reach out for help. To be open to new ideas and faces. To really think about the possibility that we will have an HIV vaccine. We will have an HIV vaccine because of our awareness, because of the need, and because of all of our efforts. Another good reason to give thanks on HVAD. Thanks to all the people I know and wish I knew who are working tirelessly in the fight against HIV.
I first wandered into a CAB meeting at the University of Colorado in 1999. The Denver site was well-established in the AIDS Clinical Trials Group (ACTG) network offering clinical trials to the HIV-infected community in the area. In the beginning we just held local monthly educational luncheons, but over the years our CAB evolved to participate in national conferences, organizing Community Educational Forums, and reviewing study protocols.

The nature of our CAB changed in the fall of 2010 when Denver was invited to become an expansion site for HVTN 505. Since our CAB was new to preventive vaccine trials, HVTN Core provided training for staff members, and for me as the Global CAB representative. The material covered was extensive and very well explained. For example, we learned about the history of vaccines as well as the past work in the HIV vaccines field.

Upon our return home we were all excited about the new project. Core lined us up with the advertising scheme: "Stand Up For Love." Our recruiter Liam was seen all over town explaining the trial, and various websites had our ads popping up. Several CAB members accompanied Liam to a booth at Gay Pride to discuss our ACTG trials and the story of ongoing vaccine research with HVTN 505. CAB members helped share the new emphasis on vaccine work with the community by organizing educational forums with input from our PI and staff.

The evolution of our CAB has been similar to many of the expansion sites that had an existing CAB. We run a joint CAB meeting on the last Friday of the month where we focus on topics that are relevant to both the ACTG and the HVTN. For our site the merging of the 2 CABs has worked smoothly. This is in part because we already had a defined protocol for how to run the meetings, specific functions for the staff, and clear rules for community members to abide by. The overall format of our meetings has stayed much the same as we have transitioned into a joint CAB. Some changes have included our outreach to new communities and bringing CAB members up to date on vaccine research. In the future we will be sending new CAB members to conferences to get them more involved and immersed in the workings of the HVTN. All of our CAB members are excited about this work.

Overall, the addition of vaccine work at the Denver site has been a great opportunity for all of us involved. The work in clinical trials has allowed us to help infected individuals with many health concerns; the addition of this vaccine work expanded this mission to finding an end to AIDS. What could be a better mission?
Dearest HVTN CAB –

Carrie Schonwald, former HVTN Community Engagement Unit-International Project Manager

By the time you read this, I imagine you will have read multiple goodbye e-mails from me and so, I am not sure that I have anything to add to what I have already said, but let me try.

I have worked in social services and public health settings for most of my career; I have been around community advocates, terrified patients, sick children and adults, and survivors of human trafficking who have lost everything imaginable. I have met officials in high places and walked in the poorest quarters of poor countries to see where sex work and HIV thrive hand in hand. I have seen the brilliant, hopeful joy of tiny children living in poverty, who are vibrant with the knowledge that they are loved. I have been inspired and I have despaired in the last five and a half years at the things I have learned and seen while working at the HVTN.

Without a doubt, the most motivating, lovely and inspiring part of my time with this organization has been meeting the Community Educators and Recruiters, CAB members, and community members who ensure that our studies have participants, and that our communities are educated, supportive, and supported. While the HVTN and NIAID conduct clinical trials at the highest possible ethical standards, our community members and educators ensure that those standards include a well-informed population, and that protocols incorporate community concerns and perspectives.

What has never ceased to amaze me in the last few years is that the vast majority of you are not only diligent and selfless in your volunteerism, but that you also tirelessly dedicate your professional lives to fighting HIV and caring for the people infected and affected by this stunning disease.

In short, you are exceptional and dear, and the world is a better place with all of you in it.

Thank you for all that you do and for sharing your luminous selves with me for the last five and a half years.

May you all thrive and may we cross paths again.

Carrie
In light of the data coming out of HVTN 505 and HVTN 503 (Phambili), it is especially helpful for community advocates to consider the range of other work that is currently being done in the HVTN, as well as plans for future studies. At the Full Group Meeting, Cecilia Morgan, of the HVTN’s Scientific Development Unit, and I presented an overview of this work.

The range of studies that are currently ongoing and planned can be thought of like a large puzzle (see page 6), with each piece contributing to the picture of our goal, a safe and effective vaccine to prevent HIV. The pieces include:

- studies currently open and enrolling,
- studies in follow-up,
- studies in development,
- observational studies,
- studies conducted in the Clade B* region,
- studies conducted in the Clade C* region,
- studies evaluating the development of specific products,
- studies building on our understanding of basic science around HIV and the immune response, and
- studies building on the results of the Thai trial (RV 144).

Within each of these pieces of the puzzle are the various studies themselves. Many studies fit into multiple categories. For example, HVTN 087 can be categorized as open & enrolling, product development, and in a Clade B region. Handouts from the session were sent out to the GCAB e-mail list after the Full Group Meeting. The handouts include a table providing a brief description of each study, including how many people will be enrolled, the sites that are participating (if known), the vaccine products being tested, the research questions being addressed, and the categories from the list above.

The important message coming out of the session was about hope! While the 503 and 505 results will shape the future of studies to come, there are many other ideas and products being tested. And it is a lot of work — we outlined 25 trials, and there are additional concepts that are currently in early stages of development, where a face-to-face meeting to write the protocol has not yet been held. It is important for the community and advocates to know that we will continue our efforts, looking to new ideas and new products to carry us forward on the path to a future preventive HIV vaccine.

* CLADE B AND C are 2 subtypes of HIV found in the world. Clade B HIV is the most common subtype of HIV in the parts of the Americas and Europe where we have sites. We also have sites in parts of South Africa where Clade C is the most common subtype.

**If you would like a copy of these handouts please email Gail, gbroder@fhcrc.org.
A Focus on Retention in the HVTN

Michele Andrasik, HVTN Social Scientist and Plenary Chair

Participant retention is an essential part of clinical trials. When participants drop out of a study, we lose information that would help us understand why a vaccine product works or not. This plenary session covered several areas of retention. The first was understanding retention data across HVTN studies. Next we looked at what has been learned in the past about retention within the HVTN. We also heard from retention experiences from the HIV Prevention Trials Network (HPTN). The panel session ended with site staff sharing what has worked for them.

As a network, we need to increase our understanding of what keeps people in a study. Looking at rates and reasons for Discontinuation of Vaccination (DOV) across the network helps us understand why people leave a study. DOVs can occur for various reasons ranging from simply “dropping-out” to becoming incarcerated or HIV infected. We found that across all studies (phase I, IIa, and IIb) the rate of DOV was 9.1% (478 individuals out of 5597 participants). In phase I and IIa studies the DOV rate was 12.4% (384 out of 3093 participants) and in the phase IIb study (HVTN 505) only 4% of participants (94 out of 2504) discontinued vaccination. Black and Latino participants had higher rates of DOV across all studies. The data showed that some of the reasons people stayed enrolled in the study was because they experienced social benefits, feeling as though their study participation might help them reduce their risk behaviors. Knowing someone with HIV infection was also related to staying in the study.

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A Focus on Retention in the HVTN

Why is retention important? High retention rates are important for study outcomes, safety and getting information to participants. We need to know the cause(s) for dropout to understand study results, and if the reasons are different for those who got the vaccine and those who did not. In HVTN 502 and HVTN 504 there was a higher loss to follow-up among HIV uninfected men. In HVTN 503 there was a greater loss to follow up among placebo participants than vaccine recipients. Special efforts are now in place to help with retention efforts for HVTN 505, which is the only vaccine efficacy study going on right now. In April of this year, the study was unblinded and participants were told if they received a vaccine or a placebo. Continuing to follow these participants is very important for HIV vaccine research. Some of these focused efforts for HVTN 505 include:

- providing clear and detailed information to participants,
- creating a welcoming site environment focusing on participant connection and contribution,
- ongoing participant communication,
- focused attention provided to participants who may be at-risk for missed visits,
- continued community engagement and education efforts.

There are also lessons that can be learned from other networks. In HPTN 061 a study looking at feasibility and acceptability of a multifaceted intervention among Black men who have sex with men (MSM), individuals who met with a peer health navigator at least once were more likely to stay in the study. The retention efforts in HPTN 061 addressed the Macro (community), Meso (site) and Micro (individual) factors that impact retention and the lessons to be learned at each level. Retention was proactively planned and individualized to ensure that the benefits of staying in the study outweighed the burden. The main take away for this presentation and the plenary overall was that retention is not a one size fits all! Individualized retention plans are key! Sites can use their knowledge and relationships with the local community to create appropriate retention plans for their participants. CAB members can help identify factors that may increase or decrease retention playing an important role in the site’s retention efforts.

HVTN’s planned and ongoing studies can be looked at like a puzzle of interconnected pieces. Many studies fall into more than 1 category working to address multiple research questions.
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participants and is on track to answer its main research questions. The DSMB can see who is getting the vaccines and who is getting the placebo. At their regularly scheduled meeting on April 22, 2013, the HVTN 505 DSMB looked at the data from the study and compared the results in people who got the vaccine to results in people who got the placebo. The results showed that the vaccine did not prevent HIV infection. The vaccine also did not reduce the viral load in those who became infected with HIV. NIAID and the study leadership agreed with the DSMB’s recommendation to stop vaccinations and moved quickly to implement this recommendation and provide participants with the information.

The HVTN 505 study enrolled 2,504 volunteers (men who have sex with men and transgender people who have sex with men) at 21 sites in 19 U.S. cities. The data examined by the DSMB was gathered from 1,250 volunteers who received the investigational vaccine regimen and 1,244 volunteers who received the placebo. In the primary analysis (which was based on those participants enrolled long enough to have received all vaccinations) 27 HIV infections occurred among the vaccine recipients, and 21 HIV infections occurred among the placebo recipients. The number of HIV infections in the investigational vaccine group compared to those in the placebo group was not statistically significant. (Read the NIH Statement for more detailed information)

Participants are being contacted by each research site to ensure they have the most up-to-date information.

The HVTN would like to follow all participants for the planned five years to maximize the ability to explain what is now known, to continue to monitor participants’ safety, and to provide ongoing HIV testing and risk reduction counseling. Each participant will have an opportunity to learn if they received vaccine or placebo. Information learned from this follow-up will inform future efforts to develop a preventive HIV vaccine.

The lack of efficacy of the vaccine regimen in HVTN 505 is a setback to all who are dedicated to the mission of finding a safe and effective HIV vaccine. However, it is only through clinical research that we will ultimately achieve this goal. The trial participants continue to be our heroes. They and the dedicated staff at the research sites must now find ways to renew their commitment in the light of this news. Together with NIAID, the HVTN and all the research site staff we will all continue to work toward our goal of finding an effective HIV vaccine.


Nashville Community Educator/Recruiter Vic Sorrell with long-time CAB member Alberta Hardison at the May 2013 HVTN Full Group Meeting.
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ABOUT CABS
Community Advisory Boards (CABs) are one way that the HVTN involves community members in the research process. CABs consist of volunteers from diverse backgrounds who work with local research units and advise them from a community perspective. Community input is invaluable to community education efforts, as well as to the development of this bulletin.

Welcome Jana!
Genevieve Meyer, Editor, HVTN CAB Bulletin

I am pleased to announce that Jana Pitzer will now be working as the assistant editor and production coordinator of the CAB Bulletin. Jana may be new to the CAB Bulletin, but she is not new to the HVTN. She started in November 2010 working as the Conference Call Coordinator. In 2011 she joined the Communications Unit and has been essential in supporting HVTN 505 with social media, print materials, advertisement purchases and placements, among other key roles. Her coordination skills have not gone unnoticed! Many of you may already be familiar with Jana, but if you have not met her she is very organized, assertive, extremely helpful, and an overall pleasure to work with.

Outside of work Jana enjoys spending time with her adorable dog “Boss,” adding to her ever expanding jewelry collection, and getting others excited about doing the same.

It is with great excitement and relief that I welcome Jana to the CAB Bulletin team.