The STEP Ezine

October 27, 2003

Issue 51

The STEP Ezine, is an electronic treatment resource newsletter distributed monthly to case managers, front-line workers, people affected by HIV/AIDS, physicians, other public health and allied health professionals and people living with HIV/AIDS. Our contact information is: STEP, a Program of Lifelong AIDS Alliance, PMB 998, 1122 East Pike Street, Seattle, WA 98122-3934, (206) 329-4857 or 1-888-399-7837.

A Special Announcement from STEP

As many of you already know, Seattle Treatment Education Project (STEP) ceased operations as an independent agency on August 9, 2003. However, we are pleased to announce that our programs continue without interruption as we have joined forces with **Lifelong AIDS Alliance** in Seattle. Now known as **STEP, a Program of Lifelong AIDS Alliance**, we are based in the headquarters of **Lifelong AIDS Alliance** on Capitol Hill. Although our physical address has changed, our mailing address remains the same:

STEP, a Program of LIFELONG AIDS Alliance
Physical address: 1002 East Seneca Street, Seattle, WA 98122
Mailing address: PMB 998, 1122 East Pike Street, Seattle, WA 98122-3934

Roberto González continues as Treatment Educator, so please contact him if you have any treatment or prevention related questions:

Email: robertog@llaa.org
Direct line: 206-957-1659
TalkLine (local): 206-329-4857
New Toll Free TalkLine (national): 1-888-399-7837

Continuing programs include our publications (*STEP Perspective*, *STEP Ezine*, *BABES Perspective*), Community Meetings, Health Management Workshops, and the STEP TalkLine. Roberto is also available by appointment for group speaking engagements and one-on-one treatment and prevention discussions.

We are also proud to announce that Quinten Welch, STEP's former Executive Director, has moved on to become the MSM Educator/Consultant with Public Health-Seattle & King County.

He can be contacted at: quinten.welch@metrokc.gov or 206-205-8671

Finally, for those of you who have supported us over the years with your kind and generous donations, we thank you and hope that you will continue to do so. If you would like to continue making tax-deductible donations in support of our programs, please make your checks payable to Lifelong AIDS Alliance and specify that the funds are for The STEP Program.

Thank you!

For further updates, call us or visit us online at www.thebody.com/step/steppage.html

NEW INNOVATIONS IN HIV PREVENTION

By Mona DePrey

The primary method of HIV transmission in the world today is through heterosexual sex. While condoms provide an effective method of prevention, many women are not able to convince their partner to use them. In many countries (including the United States) there are men who take sex as their right and do not bother to protect their partner. Often, a woman will be beaten just for suggesting their partner use a condom.

What women need is a way to protect themselves that is discreet and easy to use. Women soon may have their own secret weapon when it comes to preventing HIV transmission. Scientists at Stanford University have been working on a method that may allow women to decrease their chances of catching HIV from unsafe sex by simply inserting an inexpensive vaginal suppository once or twice a week. While the product is still a ways away from human testing, its implications for women worldwide are profound.

The technique involves using a bacterium normally present in the vagina and genetically engineering it so it expresses (makes) CD4 receptors—one of the attachment sites for HIV to enter a cell. The virus will then attach to the bacteria instead of to the cells lining the woman's vagina. The bacteria, *Lactobacillus jensenii*, are found in the mucus of a healthy vagina. Researchers took the naturally occurring bacteria and enhanced it with the gene for CD4. CD4 is found on the surface of many cells, including blood cells, as well as the cells of the vaginal lining. When HIV is first introduced into the body, it looks for and attaches to CD4. If HIV first connects or attaches to the genetically "enhanced" CD4 bacteria, the virus theoretically could be made unable to attach to the woman's own cells. Researchers so far have tested this in the laboratory. They must do animal testing before they can start human trials.

Researchers have had difficulty developing methods for women to prevent HIV transmission. The microbicides and spermicides currently available or in clinical trials have not been effective in preventing transmission and are not discreet enough to prevent detection by a partner. Female condoms are even less of a secret. This new product, if proven successful, could be inserted into the vagina as a suppository once a week to protect a woman from HIV.

The research was funded by the National Institute of Health and the Contraceptive Research and Development Program of Eastern Virginia Medical School. Lead researchers are Peter P. Lee, MD, Gary Schoolnik, MD and Mark Holodniy, MD, all of Stanford University.

WOMEN, COCAINE and HIV

A 'Babes Perspective'

Most people know that cocaine is "not good for you", but many do not know of the harmful effects cocaine has in a person infected with HIV. There have been a few studies completed in the past few years on the influence cocaine has on health when is used by someone with HIV. None of the news is good.

Cocaine users often eat poorly, have unprotected sex and neglect their health, so it has been difficult to tease out which bad effects are due to the cocaine itself and which ones are due to the habits that go along with regular drug use. Research in mice helps explain why cocaine use seems to make HIV disease progress faster and lead to more of the opportunistic infections that define AIDS. A study done at the AIDS Institute of the University of California at Los Angeles suggests that cocaine has a direct effect on HIV. Special mice were infected with HIV in human cells, then injected with either cocaine or salt water. The mice injected with cocaine increased their viral load about 200 times, even though they had a smaller number of T-helper cells than the other mice. This meant that the few T-helper cells the cocaine mice had left were churning out virus at a very high rate. It is thought the cocaine influences factors that grow more virus receptors on the T-helper cells, allowing HIV to infect them more readily.

Two other studies had results that suggested cocaine and methamphetamine use worsened AIDS-related dementia and brought about conditions in the body similar to Parkinson's disease. Parkinson's Disease is a movement disorder that includes shaking hands and an inability to control walking. Another study of gay and bisexual men (Where are the woman in HIV studies?) indicated that regular cocaine use was paired with a shorter time to death than in people who did not use cocaine.

There was also a study completed that looked at the effects of cocaine on the heart. Cocaine use in HIV negative individuals will seriously injure the heart. For instance, the young actor River Phoenix died of a heart attack brought about by cocaine use. HIV also has bad effects on the heart. The results of this study indicated that the effects of cocaine and HIV together are worse than the effects of either one alone.

In summary, research indicates that cocaine use by someone with HIV can dramatically increase her viral load, injure her brain, make dementia worse, injure her heart, and bring her to AIDS and give her opportunistic infections faster than an HIV positive woman who does not use cocaine.

Community Updates

Resources for HIV+ Women

BABES Network
Seattle, WA
206-720-5566 local
1-888-292-1912 toll free
www.babesnetwork.org

WORLD
414-13th Street, 2nd Floor
Oakland, CA 94612
510-986-0340
www.womenhiv.org

Positive Women's Network
3701 Broadway
Everett, WA 98201
425-259-9899 local
1-888-651-8931 toll free
www.pwnetwork.org

Wise Words (Project Inform)
205-13th Street, Suite 2001
San Francisco, CA 94103-2461
415-558-8669
www.projinf.org/pub/ww_index.html

Women Alive
1566 Burnside Ave.
Los Angeles, CA 90019
323-965-1564 local
1-800-554-4876 toll free hotline
www.women-alive.org

Women HIV Support Group
Pierce County AIDS Foundation
Tacoma, WA
253-383-2565
www.piercecountyaids.org

NEWS *FLASH*!!

Gilead Sciences, Inc., the manufacturer of the anti-HIV medication Tenofovir (Viread) today issued a "Dear Health Care Professional" letter (inserted below) describing high rates of virologic failure in patients treated with a "once-a-day" triple NRTI regimen that contains: Didanosine (ddI, Videx EC), Lamivudine (3TC, Epivir), and Tenofovir (Viread). This letter is somewhat technical and difficult to understand. Please call Roberto Gonzalez at 206-957-1659 or 1-888-399-7837 if you would like further explanation.

October 14, 2003

IMPORTANT DRUG WARNING

RE: High Rate of Virologic Failure in Patients with HIV Infection Treated With a Once- Daily Triple NRTI Regimen containing Didanosine, Lamivudine, and Tenofovir

Dear Health Care Professional,

Gilead Sciences, Inc (Gilead) is writing to inform you of a high rate of early virologic failure and emergence of nucleoside reverse transcriptase inhibitor (NRTI) resistance associated mutations observed in a clinical study of HIV-infected treatment-naïve patients receiving a once-daily triple NRTI regimen containing didanosine enteric coated beadlets (Videx EC, Bristol-Myers Squibb), lamivudine (Epivir, GlaxoSmithKline), and tenofovir disoproxil fumarate (Viread, Gilead).

These new data are consistent with the high rates of virologic failure observed in several recent clinical studies that have evaluated the use of triple NRTI regimens. Based on these results:

· Tenofovir DF in combination with didanosine and lamivudine is not recommended when considering a new treatment regimen for therapy-naïve or experienced patients with HIVinfection. Patients currently on this regimen should be considered for treatment modification.

In a 24-week, single-site, pilot study (N=24) designed to evaluate the safety and efficacy of a triple NRTI once-daily regimen of didanosine EC (250 mg), lamivudine (300 mg) and tenofovir DF (300 mg) in HIV-infected treatment-naïve patients, Jemsek et al. (Oral Communication, September 2003) have identified a high frequency of virologic failure (91%), which was defined as < 2 log10 reduction in plasma HIV RNA level by Week 12. Resistance testing was performed on 21 patients; 20 patients (95%) had M184I/V and 10 of these patients (50%) had K65R in addition to M184V. As a result of this high early failure rate, study enrollment was stopped.

Sub-optimal virologic response has also been reported with the use of the triple NRTI regimen abacavir/lamivudine/zidovudine (Trizivir) (Gulick 2003) and abacavir/didanosine/stavudine (Gerstoft 2003), and similarly early virologic failure and high rates of resistance mutations have been reported with abacavir/lamivudine/tenofovir DF (Farthing 2003, Gallant 2003). Overall, these studies demonstrate a lower response rate in patients on a triple NRTI regimen. Furthermore, they indicate that patients who achieve viral suppression on a triple NRTI regimen have a higher rate of virologic failure.

Reporting of Adverse Events

Please report all adverse events, following or coincident with the use of Viread, to Gilead Global Drug Safety at 1-800-GILEAD-5, option 3, or to the FDA MedWatch Program by phone (1-800-FDA-1088), by fax (1-800-FDA-0178), by mail (using postage-paid form to MedWatch, FDA, 5600 Fishers Lane, Rockville, MD 20852-9787) or via the internet at: www.accessdata.fda.gov/scripts/medwatch/http://www.accessdata.fda.gov/scripts/medwatch/

We hope this information will be helpful to you in caring for your patients. Please consult the enclosed Prescribing Information for complete product information. If you have any additional questions, please contact Gilead Medical Information toll free at 1-800-GILEAD-5, option 2.

Sincerely,

Jay Toole, MD, Ph.D.
Senior Vice President
Clinical Research

References: Farthing C, Khanlou H, Yeh V, et al. Early virologic failure in a pilot study evaluating the efficacy of once daily abacavir (ABC), lamivudine (3TC), and tenofovir DF (TDF) in treatment naïve HIV-infected patients (oral presentation). Presented at the 2nd International AIDS Society Meeting, Paris, France, July 13-16, 2003. Gallant JE, Rodriguez A, Weinberg W, et al. Early non-response to tenofovir DF (TDF) + abacavir (ABC) and lamivudine (3TC) in a randomized trial compared to efavirenz (EFV) + ABC and 3TC: ESS30009

unplanned interim analysis (oral presentation # H-1722a). Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003. Gerstoft J, Kirk O, Obel N, et al. Low efficacy and high frequency of adverse events in a randomized trial of the triple nucleoside regimen abacavir, stavudine and didanosine. AIDS 2003, 17:2045-2052. Gulick RM, Ribaudo HJ, Shikuma CM, et al. ACTG 5095: a comparative study of 3 protease inhibitor-sparing antiretroviral regimens for the initial treatment of HIV infection. 2nd IAS Conference on HIV Pathogenesis and Treatment. July 13-16, 2003. Paris. Abstract 41.

The FDA has just approved ***LEXIVA,*** a new anti-HIV medication

The Food and Drug Administration (FDA) approved, on October 20, 2003, LEXIVA (Fosamprenavir calcium), manufactured by GlaxoSmithKline and Vertex Pharmaceuticals.

LEXIVA is a prodrug of amprenavir, a protease inhibitor used to treat infection with the human immunodeficiency virus (HIV). LEXIVA is rapidly converted to amprenavir by cellular or serum phosphatases in the body.

LEXIVA should be taken in combination with other antiretroviral agents for the treatment of HIV infection in adults. The approval of LEXIVA was based on two studies in antiretroviral naïve patients and one study in protease inhibitor experienced patients.

Dr. Debra Birnkrant, director of FDA's division of antiviral products, said Lexiva offers patients a new option that allows them to reduce the number of pills they must take daily. Dosing options include taking two pills twice daily, or taking one pill twice daily with ritonavir, Birnkrant said, noting that some anti-HIV medications may require as many as eight pills twice daily. "Pill burden-wise, [Lexiva] is somewhat of an improvement, she said.

LEXIVA Tablets may be taken with or without food.

If you are on salvage therapy, talk to your doctor to see if you are a good candidate for this new medication. Note that some medications carry resistance to the same mutation; this means that if you are resistant to certain other Protease Inhibitors, you could be resistant to Lexiva. Ask your healthcare provider for more information about resistance testing.

ACKNOWLEDGEMENTS

- Please note that this is not a complete list of all HIV-related treatment information. Lifelong's STEP Program strives to provide the very latest in HIV treatment information, research and drug development information. The most current research directions and antiretroviral drug data are provided throughout the Ezine publications. You will find highlight reports as well as extensive follow-up reports from many of the AIDS research and science conferences on the Ezine. In addition, all of Lifelong's STEP Program quarterly treatment journals are available on our webpage at http://www.thebody.com/step/steppage.html or by calling our Talkline at 1-888-399-7837. Lifelong's STEP Program works hard to give unbiased treatment information to all interested parties. If you have comments, questions, suggestions or grievances, please contact step@llaa.org

Special thanks to the following for contributing written material or editing this publication

Lifelong's STEP Program Publications Advisory Committee:

Jeffrey Schouten, M.D., J.D. – Chair, Lyndsey Davis, Boyd Kravenas,
Jon Hubert, D.D.S., Janice Price, R.N., M.Ed.

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