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The Seattle Treatment Education Project's (STEP) EZINE is an electronic treatment resource distributed bi-monthly to people living with HIV/AIDS, people affected by HIV/AIDS, case Managers, front-line workers, physicians, other public health and allied health professionals. STEP's contact information is: Seattle Treatment Education Project, 1123 East John Street, Seattle, WA 98102, (206) 329-4857 or 1-877-597-STEP (WA, OR, AK, HA, ID, MT)

A STEP Conference Review of The Ninth Annual Retrovirus Conference

Held in Seattle, Washington February 24-28, 2002

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Over 3,500 researchers gathered recently in Seattle to discuss the latest laboratory and clinical advances about HIV. The main goal of the Ninth Retrovirus Conference is to facilitate translational research, or moving the latest laboratory advances into clinical research. While there were no major revolutionary findings, a lot of encouraging new information was presented in the 816 oral and poster presentations. The Conference has an excellent web site, where all the plenary sessions and symposia can be viewed in streaming video, and the abstracts searched (www.retroconference.org).

New Drugs

Two new classes of drugs in development look very encouraging. The newest class of drugs is the **integrase** inhibitors. Integrase is an enzyme used by HIV to insert its genetic message, or DNA, into cells. These compounds have been researched for years, but so far all of them have had too many side effects to move into human trials. A Japanese company, Shiongi, reported on a new integrase inhibitor called S-1360 that appears to be very potent and lacks significant side effects in animal testing. It will be moving into human trials this year.

The other class is the **entry inhibitors**, which block HIV from entering new cells. T-20 is furthest in development, but other compounds are also being developed which block other steps in the complex entry phase, including a compound called SCH C, made by Schering. HIV+ people not on any other anti-HIV drug were given SCH C for 10 days. (Unlike T-20, SCH C can be taken by mouth.) By day 3 there was a significant drop in viral load in the study participants.

A couple of presentations reviewed new data on second-generation non-nucleoside reverse transcriptase inhibitors (NNRTIs). These drugs would still be effective in people who have developed resistance to the current NNRTIs. The two drugs discussed were DPC 083 (from Bristol-Meyers Squibb) and TMC 125 (from Tibotec-Virco). DPC 083 has a modified Sustiva structure. The most common side effects were rash and some of the same central nervous system side effects as seen with Sustiva, but possibly at a lower rate. Both compounds were reported to produce up to a 1-log drop in viral load (i.e., viral loads dropped to one-tenth their

previous rates) in people who had resistance to the other NNRTIs. Larger trials are planned for both compounds to confirm these encouraging preliminary results.

Merck presented some very encouraging early Phase I studies of a new vaccine that delivers HIV genes into cells using a harmless adenovirus. These studies showed that the vaccine generated strong immunologic responses in the majority of people who received the injections. The studies are ongoing to identify the best dose before beginning larger human trials.

The first results of a large study comparing three-drug versus four-drug combinations in people with low CD4 cells or high viral load (HIV RNA) were presented. The study was conducted by the AIDS Clinical Trials Group. The three regimens compared were a protease inhibitor (PI) containing regimen, a two-PI regimen, and a PI plus a non-nucleoside drug (NNRTI). All people also received AZT and 3TC. The specific drugs used were Crixivan, Viracept and Sustiva. The group that received the PI plus the NNRTI had the best level of HIV suppression after 48 weeks.

Complications of Therapy

Several studies looked at the risk of heart attacks and strokes in people with HIV on antiretroviral therapy (ART) and found conflicting results. A large study conducted by the Centers for Diseases Control (CDC) found a higher rate of heart attacks (13 in 3,013) in people who had taken PIs, compared to those who did not take PIs (2 in 2,663). However, a very large review of veterans with HIV in the U.S from 1993 to 2001 found a large decrease in overall death rates due to the use of ART, and a slight decrease in both heart attacks and strokes over the last 8 years.

The focus on cardiovascular disease stems from the metabolic changes seen in people with HIV, especially those on antiretrovirals. Many studies tried to identify the causes of the elevated cholesterol and triglyceride levels seen in many people on ART, without any definite conclusions. *What is clear is that people with HIV infection on ART should attempt to minimize their risks for heart disease through smoking cessation, increased exercise, healthier diets, and lowering of blood fats with drug therapy, if necessary.*

Lipodystrophy Definition

We have lacked an objective, standardized definition of lipodystrophy (LD) since the syndrome was first identified approximately 5 years ago. As reported by Andrew Carr MD (Abstract 31), the European Medicines Evaluation Agency attempted to formulate a definition of LD that can be applied broadly. The 417 "cases" chosen had at least one moderate to severe rating of LD (fat loss or fat accumulation) at a particular body site identified by the person since their HIV diagnosis and was confirmed by the healthcare provider on exam

The assessment of the cases and controls included their antiretroviral and metabolic drug history, HIV disease, fasting blood test results, DEXA scan and abdominal CT (two different types of x-ray imaging that can help quantify amounts of body fat). One model was proposed that included the following as indicating LD: a low trunk-to-peripheral-fat ratio and low percentage of leg fat by DEXA, report of abdominal bloating, lower alcohol consumption, higher waist-to-hip ratio, higher total-to-HDL cholesterol ratio, higher anion gap, report of increased bleeding tendency, higher intra-abdominal to extra-abdominal fat ratio by CT, and greater age. This model had a sensitivity of 84.4 percent (i.e., using this model, about 84 percent of the cases would be detected) and specificity of 81.4 percent (of the cases detected, only 81 percent of them would truly have LD). Unfortunately, definitions using only DEXA and CT or only labs were even less sensitive and specific.

Carr concluded that this model can diagnose HIV LD "simply and objectively" and the research team plans to make a scoring system available on the Internet to help healthcare providers diagnose LD in practice. It remains to be seen if this new definition, which is not all that simple, is clinically useful. The assessments used in the model, such as DEXA and CT scan, are often not used in clinical practice, because they are costly and their interpretation is not well standardized. Thus, although a step in the right direction, this definition for LD might be more useful for future research studies than for practice. Validation for the definition is still necessary as well.

Lipodystrophy: To Switch or Not to Switch?

The etiology of LD also remains in debate, which contributes to the difficulty of defining the syndrome. Various antiretroviral drugs have been implicated in the body changes and metabolic derangements associated with LD. "Switch" studies were presented at the Ninth Retrovirus Conference to determine if swapping one drug, used as part of a highly active anti-retroviral therapy (HAART) regimen, for another, would improve LD.

The NRTIs have been implicated as a cause of LD, mainly fat loss (lipoatrophy). Of the NRTIs, Zerit is thought most frequently to be the culprit. Studies adding NRTIs to regimens have noted an increase in the frequency of LD over time (Abstract 683). An earlier study conducted in France by T. Saint-Marc evaluated the switch from Zerit to either AZT or Ziagen in persons with lipoatrophy and found statistically significant improvements in subcutaneous fat in the abdomen and legs.

Three switch studies presented at this year's Ninth Retrovirus Conference confirm the improvement in body shape, but found that the amount of improvement is likely not clinically significant.

The first of these switch studies randomized 111 participants with moderate to severe lipoatrophy on Zerit or AZT with an undetectable viral load to either continue their therapy or switch to Ziagen (Abstract 32). After the switch to Ziagen, virologic control was maintained. After 24 weeks there were very small statistically significant increases in limb and abdominal subcutaneous fat. However, these increases were not clinically significant (they could not be seen with the naked eye). Of note, the people who continued their original regimen did not have progression of their lipoatrophy and switching to Ziagen for the minimal improvements seen was associated with a 10 percent risk of hypersensitivity.

The other two similar NRTI switch studies also compared people on a Zerit-containing regimen to people who switched to other NRTIs such as AZT, Ziagen or Trizivir (Abstracts 700, 701). Using DEXA scans, both studies demonstrated small improvements in subcutaneous fat that was greater in the arms than in the legs. Of note, fat changes in the face were not addressed in any of these studies.

Taken together, these switch studies do provide confirmation that Zerit is likely responsible for at least some of the lipoatrophy observed in people. A switch to Ziagen appears to stop further fat loss and indeed resulted in slow and modest improvement in subcutaneous fat levels. Yet none of these studies had dramatic, or even clinically significant increases in fat. Participants and healthcare providers were unable to actually appreciate the changes detected by the imaging techniques used. The lack of significant improvement of fat levels could indicate long-term irreversible toxicity of the medications used, it may just mean either longer follow-up is needed, or that there are other yet unidentified factors contributing to the fat loss. In practice, Zerit has been generally well tolerated and easy to take. The minimal improvements with switching to another drug may not be worth the risk of toxicity and losing control of the HIV, although in the people studied there was continued viral suppression after the switch to Ziagen.

PIs have also been implicated in the development of LD, but mostly with fat accumulation rather than fat loss. They are thought to play a role in causing the metabolic changes (increased blood sugar and cholesterol) seen with HAART, as well as the changes in body shape. A large number of case reports and several studies have looked at the effect of switching from a PI-containing regimen to a PI-sparing regimen on cholesterol, triglycerides and body shape changes. Two studies presented at the Ninth Retrovirus Conference this year randomized people on a PI-containing regimen with stable viral suppression to either Ziagen, Sustiva or Viramune (Abstracts 17, 699).

Switching from a PI to an NNRTI is associated with metabolic improvements (decreases in bad cholesterol and improvements in good cholesterol). It is assumed that improved lipid profiles mean a decreased risk of heart disease and other vascular complications, because this has been clearly shown in HIV- people who lower their cholesterol. Changing regimens to decrease cholesterol will be most important in people with known heart disease or other cardiac risk factors. For those with no risk factors and only modest elevations of cholesterol it is not clear that changing antiviral regimens is necessary. *Switches to Ziagen are less safe from the virologic point of view, especially if someone has extensive prior nucleoside experience, but better tolerated in regard to side effects.*

Reversal of abnormalities in glucose and lipid metabolism when the PIs are replaced with an NNRTI or Ziagen (when viremia remains undetectable) supports the conclusion that PIs are, at least in part, responsible for these metabolic changes. The lack of significant improvement in body fat redistribution after switching from Zerit or a PI-containing regimen suggests that the causes of changes in body habitus are more complex. Other studies have implicated host factors, such as race, as well as disease factors such as viral suppression, history of low CD4 count, and change in CD4 count in the development of LD.

Lipodystrophy Treatment

Without knowing the actual cause, treatment of LD remains difficult. There has been considerable interest in using "glitazones" (a class of drug used for diabetes) in the treatment of LD after two small studies had some promising results. The glitazones in general work by increasing the body's sensitivity to insulin, and in some diabetics can lead to weight gain and reduction in the LDL (the bad cholesterol). In the lab, rosiglitazone, one of the drugs from this class, prevents some of the deleterious effects of PIs, providing the rationale for using it in the treatment of HIV-related LD (Abstract 690). *Unfortunately, very disappointing results were presented from the first prospective, randomized trial using high-dose rosiglitazone in 30 HIV+ people with LD (Abstract 13).* At 24 weeks, although there was improvement in insulin resistance, there was no difference in either weight or fat mass between those who took rosiglitazone and those who took placebo. Several people, surprisingly, developed severe hyperlipidemia on rosiglitazone therapy, which caused one person to stop taking the drug. Despite the small sample size, the future of rosiglitazone as a treatment for HIV-associated LD does not look promising. Treatment with gemfibrozil and metformin (two other diabetic medications) did not look promising either (Abstract 702). More studies are certainly needed to better determine the causes of LD in order to develop better treatments for the syndrome.

Structured Treatment Interruptions

The benefit of structured treatment interruptions (STIs) for HIV has been the subject of a lot of debate. Interrupting antiretroviral treatment is an enticing idea to many people living with HIV and to healthcare providers. STIs would limit drug exposure and therefore decrease drug toxicity, drug costs, and possibly decrease drug resistance and failure rates. It was thought that STIs would also lead to "autovaccination" and boost anti-HIV immunity, as a result of repeated episodes of recurrent HIV in the blood (viremia), which in turn would result in persistent low HIV viral loads (VL) even off therapy. Unfortunately, small studies have resulted

in disappointing results. Autovaccination, although it may be helpful in acute HIV infection, does not appear to improve HIV-related immunity in the chronically infected patient. *More importantly, STIs resulted in a risk of significant declines in CD4 cell counts.*

Bernard Hirscel presented the results of one of the largest cohorts of chronically infected HIV+ people (133) who have undergone STIs in the Swiss and Spanish Intermittent Treatment Trial (SSITT) (Abstract 528). Individuals were on stable HAART therapy (no NNRTIs used) with a suppressed virus load for at least 6 months and a CD4+ cell count above 300. Participants underwent four cycles in which HAART was alternately stopped for 2 weeks and then restarted for 8 weeks. Treatment was then discontinued indefinitely at week 40. Participants were allowed to restart HAART if pre-determined thresholds for virus load and CD4+ cell counts were exceeded. Viral "rebound" was defined as a load above 200 copies/mL and viral "response" was defined as a load below 5000 copies at 52 weeks.

Eighty-eight of 133 participants had a rebound after the first 2 weeks of interrupted treatment. Only 17 percent of the participants responded at week 52 which declined to 11 percent by week 96. Forty-nine patients remained off HAART after a median of 44 weeks. CD4 cell counts declined by 175 cells/mm^3 during the first 12 weeks off treatment and then stabilized. In all patients except one, the viral load was promptly resuppressed when the previous HAART regimen was resumed. HIV-specific immunity increased by week 52, but did not correlate with response. *This study, along with many others, disproved the benefit of autovaccination, since the patients with greater anti-HIV immune responses actually had higher viral rebounds.*

The authors concluded that a number of patients with HIV infection on suppressive HAART could be safely managed off HAART for several months, but that STIs alone are rarely enough to maintain a low viral load when HAART is stopped. It is clear that STIs were not effective in controlling HIV infection in the majority of patients. However, the measure of success is dependent on the goals of treatment. The patients in this study were able to be off HAART for several months with prompt resuppression of their HIV after resuming HAART, making drug holidays a viable option to diminish side effects and costs. However, these patients all suffered a substantial drop in their CD4+ cell counts.

Jens Lundgren, from the EuroSIDA cohort study, reported new and interesting data on the risk of developing a new AIDS-defining event after interrupting or stopping HAART (Abstract 48). Of 5,385 patients who initiated HAART, 776 patients (20 percent) interrupted treatment for a multitude of reasons, although 518 of these patients re-initiated therapy sometime later. These drug interruptions were not scheduled or structured. The rate of HAART interruption was 21 percent for every 5 years and was more frequent in women and IV drug users. During the first 3 months off HAART there was a median drop in the CD4+ cell count of 30 cells, and an increase in the HIV viral load of 1 log (a 10-fold increase). Significant progression of clinical disease off HAART increased by more than five times, especially in patients with low CD4+ cell counts (i.e., people with a CD4+ cell count below 50 had an 80 percent risk of developing an AIDS-defining illness off therapy compared to only a 30 percent chance on HAART). It appears that HAART has a beneficial clinical effect not explained by the CD4 cell count and the HIV viral load even when treatment is failing. *This data also suggests that STIs are not clinically safe in patients with low CD4 cell counts.*

Other prospective, controlled studies are in progress. These are looking at different STI schedule strategies (such as determining interruptions by the calendar, by a threshold CD4 cell count, by viral load, or by comparing long and short interruptions) and evaluating STI in combination with additional immune stimulatory maneuvers (such as vaccines and cytokines). These studies will help to determine if STIs are a reasonable strategy to reduce long-term exposure to antiretrovirals, thereby decreasing associated costs and side effects.

HIV/HCV Co-Infection

Hepatitis C (HCV) affects 40 to 175 million people worldwide and 3 million people in the U.S. alone. Hepatitis C directly infects the liver cells and it is unknown whether liver damage is due to the direct effects of the virus, the person's immune-mediated response, or more likely, both. Unlike hepatitis B, HCV has no virological latency (the virus does not incorporate into the host cell's DNA) and therefore it is one of the few chronic viral infections that are potentially a curable disease. There are six major HCV genotypes (species) worldwide. In the U.S., more than 75 percent of the people with HCV have genotype 1, which, unfortunately, is the most difficult genotype to treat, because it does not respond as well to the current therapies available.

In patients with HIV, higher HCV viral loads are associated with an increased risk of HCV transmission and accelerated liver disease (Abstract 657). Co-infection with HIV and HCV is frequent given the shared routes of infection (e.g., IV drug use, sexual contact, blood contact). Increased survival in HIV+ people, since the era of HAART, has made morbidity and mortality from HCV of increased importance. Potential benefits of treatment for HCV in HIV+ people not only includes delaying progression of liver disease, but may also include improvement in the tolerability and possibly the effectiveness of HAART. HAART causes flares in the liver enzymes (ALT and AST) in people with HCV and people with HCV have a two- to four-fold risk of liver toxicity due to HAART (e.g., Viramune) (Abstract 662). There was also some concern that HCV accelerates HIV progression, but this has not been shown to be true. Of note, it is important for all people with HIV/HCV co-infection to get vaccinated for hepatitis A and to limit their alcohol intake.

The combination of interferon (IFN) with ribavirin has a decreased sustained viral response rate in HIV+ compared to HIV- people. Studies using IFN daily rather than three times per week have had better success rates, but the discontinuation rates were higher (up to 23 percent) (Abstract 651). Theories for why response rates are less in HIV/HCV co-infected people include the higher discontinuation rates, a poorer immune response to HCV, increased HCV levels, more inaccessible reservoirs of HIV (compartmentalization) and altered cytokines. However, in all studies, HIV control was maintained throughout HCV therapy.

Pegylated-IFN (Peg-IFN) has a longer half-life than regular IFN, which results in better overall sustained virologic response rates in both HIV- and HIV+ individuals. Peg-IFN with Ribavirin has become the standard of care for chronic HCV. HCV clearance is slower in HIV/HCV patients, so HIV+ patients may need to be treated longer to ensure sustained response rates similar to HCV mono-infection.

ACTG trial 5071 was a prospective multicenter trial of IFN with ribavirin compared to peg-IFN with ribavirin for 134 HCV/HIV co-infected patients (Abstract LB15). If there was virological response by week 24, treatment was continued through 48 weeks. The preliminary 24-week HCV viral suppression rate for IFN with ribavirin was 15 percent compared to 44 percent for peg-IFN with ribavirin (comparable to the sustained response rates in HIV- people). The response rates were, as predicted, worse with genotype 1 virus (7 percent vs. 33 percent) and better with non-genotype1 virus (40 percent vs. 80 percent). These results are very preliminary, and need to be followed to see what the sustained viral suppression rate is after the interferon is stopped.

Another study of peg-IFN with ribavirin in 65 HIV+ subjects with chronic HCV revealed that the regimen is relatively well tolerated in people on HAART, with only a 14 percent discontinuation rate (Abstract 652). There was a response in 50 percent of patients, but in only 33 percent was the response sustained over time. A reduction in the ribavirin dose was necessary in 3 percent of the patients due to toxicities. One patient on Videx developed pancreatitis, and 3 percent of patients had a significant decrease in their CD4 count during the study, which may or may not have been related to the HCV treatment.

A last resort treatment for HCV and end-stage liver disease is liver transplant. A study of 23 HIV+ patients, from four major transplant centers, showed comparable survival to HIV- people undergoing liver

transplantation. HCV infection was the most common reason for the transplant. Deaths following liver transplantation in HIV+ recipients were found to be strongly associated with the inability to tolerate HAART after transplantation (Abstract 125). Additional experience with liver transplants in HIV+ people is needed before definitive recommendations can be made about its indications. *However, the blanket exclusion of HIV+ people from most liver transplant centers can no longer be scientifically justified.*

HIV/HBV Co-Infection

A total of 300 million people worldwide are infected with hepatitis B virus (HBV). Of people with HIV, 70 to 90 percent have a history of HBV exposure and 10 to 15 percent have chronic HBV infection. It has been found that people with HIV have higher HBV DNA levels (evidence of more virus present) secondary to an inadequate immune response, about a 10-fold increased mortality secondary to liver disease compared to people with HBV alone (Abstracts 656, 657), and an increased risk of liver inflammation (hepatotoxicity) associated with antiretrovirals (e.g. Viramune) (Abstract 662). Thus, recognition of HIV/HBV co-infection and focusing on treatment of both viruses simultaneously is of growing importance.

Liver disease associated with HBV is not due to direct effects of the virus on the liver cells, but is instead due to damage from the host's immune response to the HBV. Therefore, in people with HIV/HBV co-infection who are very immunosuppressed and who do not have an active immune response, there is little to no liver damage but high HBV DNA levels. On the other hand, when the HIV is controlled with HAART and the immune system is restored, there is subsequent liver damage with an increase of the liver enzymes as a result of immune reconstitution. This demonstrates the importance of not treating HIV alone but instituting treatment of HBV at the same time as HIV, since HAART may induce reactivation hepatitis as the HIV is suppressed. It is also important not to treat HBV alone either, since it can result in resistance of the HIV virus to the drugs used to treat HBV (e.g., Epivir, Viread, adefovir).

Dr. Marion Peters in her lecture on HBV stressed that the best treatment for HBV is prevention with the vaccine. Unfortunately, only 12 percent of HIV+ people are currently being vaccinated for hepatitis A and HBV. It is also important to remember that although immunity against HBV after receiving the vaccine lasts about 10 to 15 years in HIV- people, it is unclear how long it is effective in HIV+ people. *It is recommended that people with HIV have their HBV immunity levels checked yearly and get re-vaccinated if their HBV antibody level is below 10u/ml.*

Very exciting data was presented at the Ninth Retrovirus Conference on new drugs to treat HBV in co-infected individuals. Dr. David Thomas reviewed the use of IFN and Epivir and then preliminary data using adefovir and Viread was discussed. Success of treatment is measured by decreased levels of HBV DNA viral load, decreased liver enzymes, and histologic improvement on biopsy.

IFN alpha 2a or 2b is given as 5 million units subcutaneously (under the skin) every day, or 10 million units three times a week. In one study, HBV DNA became undetectable in about 35 percent treated with IFN, compared to approximately 15 percent of the controls. There is now very early data showing that the use of the newer formulation of IFN, pegylated IFN, may have better results. However, IFN has not been well studied in HIV+ people.

Epivir, an NRTI, is also used for the treatment of HBV, especially in people with decompensated cirrhosis (severe liver scarring), when IFN is contraindicated. It has a very high rate of success that is similar in HIV+ and HIV- subjects. Greater than 90 percent of people treated with Epivir suppress their HBV DNA, but unfortunately, resistance develops at a rate of 20 percent of people per year (Abstract 673). After 4 years, about 90 percent of HIV/HBV co-infected people are Epivir resistant (Abstract 123). Also, Epivir only decreases HBV DNA levels in the blood, it does not completely eliminate the virus, so when treatment stops, the virus

often returns eventually. There have been some studies looking at using IFN and Epivir together, but only about 29 percent of study participants cleared the virus. This is why new treatments are needed to treat HBV in both the HIV- and HIV+ individuals.

Two promising options in the treatment of HBV are adefovir and Viread, both of which are effective not only against wild-type virus (virus without any mutations) but also virus that is already resistant to Epivir. Both drugs decreased the HBV DNA by similar amounts at 24 weeks, but additional data is necessary to determine long-term outcomes.

Adefovir 10 mg once daily was started in 35 HIV/HBV co-infected people (34 male, 1 female) who were already on Epivir as part of their HAART regimen (Abstract 123). All the people had developed Epivir resistance mutations with detectable HBV DNA in their blood. The drug was well tolerated and no people had HBV DNA rebound during the 72 weeks of treatment. There was no kidney damage seen, as had been observed in studies using higher doses of adefovir (60 to 120 mg) in HIV trials. In HIV/HBV co-infected people, adefovir resulted in a continued decline of the serum HBV DNA at 72 weeks and histologic improvement. (In the biopsies done, there was a decrease in the amount of inflammation and fibrosis.) However, there was no significant change in the CD4 cell count with the addition of low dose adefovir to the HAART regimen.

Viread, 300 mg once daily, was also added to a stable regimen of HAART in HIV/HBV co-infected people in a double blinded, placebo controlled study of 14 people (12 Viread, 2 placebo) (Abstract 124). Viread was well tolerated. Preliminary analysis at 24 weeks reveals a significant decrease in the HBV DNA of both wild-type and Epivir-resistant virus in HIV/HBV co-infected people. There was a slight decrease in the HIV RNA in people treated with Viread, as well.

Other treatments for HBV are currently being evaluated, including entecavir, ribozymes, immunotherapy, L-dT, and liver transplant. Hopefully, with continued research there will be better treatments for co-infected individuals soon.

Dr. Jeff Schouten is Chair of STEP's Publications Committee, and an Attending Physician at Harborview's Madison Clinic. Dr. Lara Strick is a member of STEP's Board of Directors, and is completing her residency in internal medicine at the University of Washington.

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- Please note that this is not a complete list of all HIV-related treatment information. STEP 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 STEP quarterly treatment journals are available on our Web site at http://www.thebody.com/step/steppage.html or by calling our Talkline at 1-877-597-STEP. STEP works hard to give unbiased treatment information to all interested parties. If you have comments, questions, suggestions or grievances, please contact robertog@stepproject.org or ezine@stepproject.org.

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