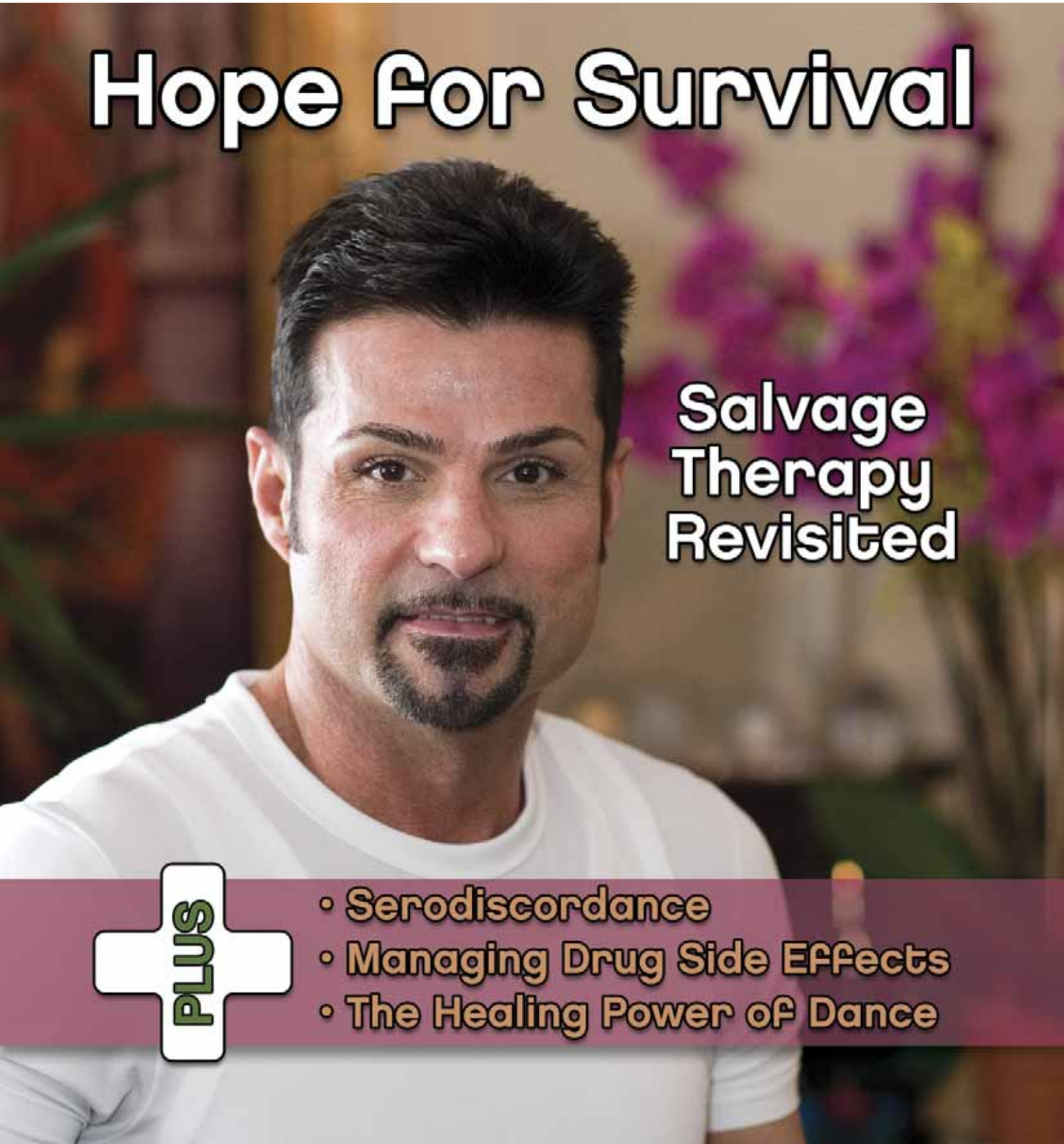
March / April 2007

Positively Aware

The Journal of Test Positive Aware Network



Important Information

INDICATION: ATRIPLA™ (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) is a prescription medication used alone as a complete regimen or with other medicines to treat HIV infection in adults.

ATRIPLA does not cure HIV or prevent passing HIV to others. See your healthcare provider regularly.

IMPORTANT SAFETY INFORMATION:

Contact your healthcare provider right away if you experience any of the following side effects or conditions associated with ATRIPLA:

- **Nausea, vomiting, unusual muscle pain, and/or weakness. These may be signs of a buildup of acid in the blood (lactic acidosis), which is a serious medical condition.**
- **Light colored stools, dark colored urine, and/or if your skin or the whites of your eyes turn yellow. These may be signs of serious liver problems.**
- **If you have HIV and hepatitis B virus (HBV), your liver disease may suddenly get worse if you stop taking ATRIPLA. Do not stop taking ATRIPLA unless directed by your healthcare provider.**

Do not take ATRIPLA if you are taking the following medicines because serious and life-threatening side effects may occur when taken together: Hismanal® (astemizole), Propulsid® (cisapride), Versed® (midazolam), Halcion® (triazolam), or ergot derivatives (for example, Wigraine® and Cafergot®).

In addition, ATRIPLA should not be taken with: Combivir® (lamivudine/zidovudine), Emtriva® (emtricitabine), Epivir® or Epivir-HBV® (lamivudine), Epzicom™ (abacavir sulfate/lamivudine), Sustiva® (efavirenz), Trizivir® (abacavir sulfate/lamivudine/zidovudine), Truvada® (emtricitabine/tenofovir disoproxil fumarate [DF]), or Viread® (tenofovir DF), because they contain the same or similar active ingredients as ATRIPLA.

Vfend® (voriconazole) should not be taken with ATRIPLA since it may lose its effect or may increase the chance of having side effects from ATRIPLA. Fortovase®, Invirase® (saquinavir mesylate) should not be used as the only protease inhibitor in combination with ATRIPLA.

Taking ATRIPLA with St. John's wort *(Hypericum perforatum)* is not recommended as it may cause decreased levels of ATRIPLA, increased viral load, and possible resistance to ATRIPLA or cross-resistance to other anti-HIV drugs.

This list of medicines is not complete. Discuss with your healthcare provider all prescription and nonprescription medicines, vitamins, and herbal supplements you are taking or plan to take.

Contact your healthcare provider right away if you experience any of the following side effects or conditions:

- **Severe depression, strange thoughts, or angry/abnormal behavior** have been reported by a small number of patients. Some patients have had thoughts of suicide and a few have actually committed suicide. These problems may occur more often in patients who have had mental illness.
- **Dizziness, trouble sleeping or concentrating, drowsiness, unusual dreams, and/or hallucinations** are common, and tend to go away after taking ATRIPLA™ (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) for a few weeks. Symptoms were severe in a few patients and some patients discontinued therapy. These symptoms may become more severe with the use of alcohol and/or mood-altering (street) drugs. If you are dizzy, have trouble concentrating, and/or are drowsy, avoid activities that may be dangerous, such as driving or operating machinery.
- **Kidney or liver problems.** If you have had kidney or liver problems, including hepatitis infection or take other medicines that may cause kidney or liver problems, your healthcare provider should do regular blood tests.
- **Pregnancy: Women should not become pregnant while taking ATRIPLA.** Serious birth defects have been seen in children of women treated during pregnancy with one of the medicines in ATRIPLA. Women must use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control.
- **Breast-Feeding: Women with HIV should not breast-feed** because they can pass HIV through their milk to the baby. Also, ATRIPLA may pass through breast milk and cause serious harm to the baby.
- **Rash** is a common side effect that usually goes away without treatment, but may be serious in a small number of patients.
- **Seizures** have occurred in patients taking a component of ATRIPLA, usually in those with a history of seizures. If you have ever had seizures, or take medicine for seizures, your healthcare provider may want to monitor you.
- **Bone changes.** If you have had bone problems in the past, your healthcare provider may want to check your bones.
- **If you have ever had mental illness or use illegal drugs or alcohol.**

Changes in body fat have been seen in some people taking anti-HIV medicines. The cause and long-term health effects are not known.

Common side effects of ATRIPLA include tiredness, headache, upset stomach, vomiting, gas, and diarrhea. Skin discoloration (small spots or freckles) may also happen with ATRIPLA.

You should take ATRIPLA once daily on an empty stomach. Taking ATRIPLA at bedtime may make some side effects less bothersome.

If you or someone you know needs help paying for medicine, call 1-888-4PPA-NOW (1-888-477-2669). Or go to www.pparx.org

Partnership for Prescription Assistance

Bristol-Myers Squibb GILEAD

The first and only complete HIV regimen in one pill daily. ATRIPLA may be taken alone or with other HIV medicines.

- **Effective:** Proven to lower viral load to undetectable† and help raise T-cell (CD4+) count through 48 weeks of a clinical study.
- **One Pill, Once a Day:** Take on an empty stomach, preferably at bedtime, and you're done with ATRIPLA for 24 hours. Taking ATRIPLA at bedtime may make some side effects less bothersome.
- **Tolerability:** Well-established patient experience in clinical studies with the three proven medicines in ATRIPLA.

† Undetectable was defined as a viral load of less than 400 copies/mL.

ATRIPLA™
(efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) Tablets

It all adds up to one.™ *

Ask your doctor if ATRIPLA is right for you.

visit www.ATRIPLA.com

* ATRIPLA is a combination of 3 HIV medicines – SUSTIVA® (efavirenz), EMTRIVA® (emtricitabine), and VIREAD® (tenofovir disoproxil fumarate)

Please see Patient Information including "What is the most important information I should know about ATRIPLA?" on the next page.

PATIENT INFORMATION

℞ **ONLY**

ATRIPLA™ (uh TRIP luh) Tablets

ALERT: Find out about medicines that should NOT be taken with ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg).

Please also read the section **"MEDICINES YOU SHOULD NOT TAKE WITH ATRIPLA."**

Generic name: efavirenz, emtricitabine and tenofovir disoproxil fumarate (eh FAH vih renz, em tri SIT uh bean and te NOE' fo veer dye soe PROX il FYOU mar ate)

Read the Patient Information that comes with ATRIPLA before you start taking it and each time you get a refill since there may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. You should stay under a healthcare provider's care when taking ATRIPLA. **Do not change or stop your medicine without first talking with your healthcare provider.** Talk to your healthcare provider or pharmacist if you have any questions about ATRIPLA.

What is the most important information I should know about ATRIPLA?

- **Some people who have taken medicine like ATRIPLA (which contains nucleoside analogs) have developed a serious condition called lactic acidosis** (build up of an acid in the blood). Lactic acidosis can be a medical emergency and may need to be treated in the hospital. **Call your healthcare provider right away if you get the following signs or symptoms of lactic acidosis:**
  - You feel very weak or tired.
  - You have unusual (not normal) muscle pain.
  - You have trouble breathing.
  - You have stomach pain with nausea and vomiting.
  - You feel cold, especially in your arms and legs.
  - You feel dizzy or lightheaded.
  - You have a fast or irregular heartbeat.
- **Some people who have taken medicines like ATRIPLA have developed serious liver problems called hepatotoxicity,** with liver enlargement (hepatomegaly) and fat in the liver (steatosis). **Call your healthcare provider right away if you get the following signs or symptoms of liver problems:**
  - Your skin or the white part of your eyes turns yellow (jaundice).
  - Your urine turns dark.
  - Your bowel movements (stools) turn light in color.
  - You don't feel like eating food for several days or longer.
  - You feel sick to your stomach (nausea).
  - You have lower stomach area (abdominal) pain.
- **You may be more likely to get lactic acidosis or liver problems** if you are female, very overweight (obese), or have been taking nucleoside analog-containing medicines, like ATRIPLA, for a long time.
- **If you also have Hepatitis B Virus (HBV) infection and you stop taking ATRIPLA, you may get a "flare-up" of your hepatitis. A "flare-up" is when the disease suddenly returns in a worse way than before.** Patients with HBV who stop taking ATRIPLA need close medical follow-up for several months, including medical exams and blood tests to check for hepatitis that could be getting worse. ATRIPLA is not approved for the treatment of HBV, so you must discuss your HBV therapy with your healthcare provider.

What is ATRIPLA?

ATRIPLA contains 3 medicines, SUSTIVA® (efavirenz), EMTRIVA® (emtricitabine) and VIREAD® (tenofovir disoproxil fumarate also called tenofovir DF) combined in one pill. EMTRIVA and VIREAD are HIV (human immunodeficiency virus) nucleoside analog reverse transcriptase inhibitors (NRTIs) and SUSTIVA is an HIV non-nucleoside analog reverse transcriptase inhibitor (NNRTI). VIREAD and EMTRIVA are the components of TRUVADA®. ATRIPLA can be used alone as a complete regimen, or in combination with other anti-HIV medicines to treat people with HIV infection. ATRIPLA is for adults age 18 and over. ATRIPLA has not been studied in children under age 18 or adults over age 65.

HIV infection destroys CD4 (T) cells, which are important to the immune system. The immune system helps fight infection. After a large number of T cells are destroyed, acquired immune deficiency syndrome (AIDS) develops.

ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) helps block HIV reverse transcriptase, a viral chemical in your body (enzyme) that is needed for HIV to multiply. ATRIPLA lowers the amount of HIV in the blood (viral load). ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) may also help to increase the number of T cells (CD4 cells), allowing your immune system to improve. Lowering the amount of HIV in the blood lowers the chance of death or infections that happen when your immune system is weak (opportunistic infections).

Does ATRIPLA cure HIV-1 or AIDS?

ATRIPLA does not cure HIV infection or AIDS. The long-term effects of ATRIPLA are not known at this time. People taking ATRIPLA may still get opportunistic infections or other conditions that happen with HIV infection. Opportunistic infections are infections that develop because the immune system is weak. Some of these conditions are pneumonia, herpes virus infections, and *Mycobacterium avium complex* (MAC) infection. **It is very important that you see your healthcare provider regularly while taking ATRIPLA.**

Does ATRIPLA reduce the risk of passing HIV-1 to others?

ATRIPLA has not been shown to lower your chance of passing HIV to other people through sexual contact, sharing needles, or being exposed to your blood.

- **Do not share needles or other injection equipment.**
- **Do not share personal items that can have blood or body fluids on them, like toothbrushes or razor blades.**
- **Do not have any kind of sex without protection.** Always practice safer sex by using a latex or polyurethane condom or other barrier to reduce the chance of sexual contact with semen, vaginal secretions, or blood.

Who should not take ATRIPLA?

Together with your healthcare provider, you need to decide whether ATRIPLA is right for you.

Do not take ATRIPLA if you are allergic to ATRIPLA or any of its ingredients. The active ingredients of ATRIPLA are efavirenz, emtricitabine, and tenofovir DF. See the end of this leaflet for a complete list of ingredients.

What should I tell my healthcare provider before taking ATRIPLA?

Tell your healthcare provider if you:

- **Are pregnant or planning to become pregnant** (see "What should I avoid while taking ATRIPLA?").
- **Are breast-feeding** (see "What should I avoid while taking ATRIPLA?").
- **Have kidney problems or are undergoing kidney dialysis treatment.**
- **Have bone problems.**
- **Have liver problems, including Hepatitis B Virus infection.** Your healthcare provider may want to do tests to check your liver while you take ATRIPLA.
- **Have ever had mental illness or are using drugs or alcohol.**
- **Have ever had seizures or are taking medicine for seizures.**

What important information should I know about taking other medicines with ATRIPLA?

ATRIPLA may change the effect of other medicines, including the ones for HIV, and may cause serious side effects. Your healthcare provider may change your other medicines or change their doses. Other medicines, including herbal products, may affect ATRIPLA. For this reason, **it is very important to** let all your healthcare providers and pharmacists know what medications, herbal supplements, or vitamins you are taking.

MEDICINES YOU SHOULD NOT TAKE WITH ATRIPLA

- The following medicines may cause serious and life-threatening side effects when taken with ATRIPLA. You should not take any of these medicines while taking ATRIPLA: Hismanol® (astemizole), Propulsid® (cisapride), Versed® (midazolam), Halcion® (triazolam), ergot medications (for example, Wigraine® and Cafergot®).
- ATRIPLA also should not be used with COMBIVIR®, EMTRIVA, EPIVIR®, EPIVIR-HBV®, EPZICOM™, TRIZIVIR®, SUSTIVA, TRUVADA®, or VIREAD.
- Vfend® (voriconazole) should not be taken with ATRIPLA since it may lose its effect or may increase the chance of having side effects from ATRIPLA.

It is also important to tell your healthcare provider if you are taking any of the following:

- Fortovase®, Invirase® (saquinavir), or Biaxin® (clarithromycin); **these medicines may need to be replaced with another medicine when taken with ATRIPLA.**
- Crixivan® (indinavir); Methadone; Mycobutin® (rifabutin); Rifampin; cholesterol-lowering medicines such as Lipitor® (atorvastatin), PRAVACHOL® (pravastatin), and Zocor® (simvastatin); or Zoloft® (sertraline); **these medicines may need to have their dose changed when taken with ATRIPLA.**
- Videx®, Videx® EC (didanosine); tenofovir DF (a component of ATRIPLA) may increase the amount of didanosine in your blood, which could result in more side effects. **You may need to be monitored more carefully** if you are taking ATRIPLA and didanosine together. Also, the dose of didanosine may need to be changed.
- Reyataz® (atazanavir sulfate) or Kaletra® (lopinavir/ritonavir); these medicines may increase the amount of tenofovir DF (a component of ATRIPLA) in your blood, which could result in more side effects. **You may need to be monitored more carefully** if you are taking ATRIPLA and either Reyataz or Kaletra together. Also, the dose of Reyataz or Kaletra may need to be changed.
- Medicine for seizures [for example, Dilantin® (phenytoin), Tegretol® (carbamazepine), or phenobarbital]; your healthcare provider may want to switch you to another medicine or check drug levels in your blood from time to time.
- **Taking St. John's wort *(Hypericum perforatum),* or products containing St. John's wort with ATRIPLA is not recommended.** St. John's wort is a herbal product sold as a dietary supplement. Talk with your healthcare provider if you are taking or are planning to take St. John's wort. Taking St. John's wort may decrease ATRIPLA levels and lead to increased viral load and possible resistance to ATRIPLA or cross-resistance to other anti-HIV drugs.

These are not all the medicines that may cause problems if you take ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/ tenofovir disoproxil fumarate 300 mg). Be sure to tell your healthcare provider about all medicines that you take.

Keep a complete list of all the prescription and nonprescription medicines as well as any herbal remedies that you are taking, how much you take, and how often you take them. Make a new list when medicines or herbal remedies are added or stopped, or if the dose changes. Give copies of this list to all of your healthcare providers and pharmacists **every** time you visit your healthcare provider or fill a prescription. This will give your healthcare provider a complete picture of the medicines you use. Then he or she can decide the best approach for your situation.

How should I take ATRIPLA?

- Take the exact amount of ATRIPLA your healthcare provider prescribes. Never change the dose on your own. Do not stop this medicine unless your healthcare provider tells you to stop.
- You should take ATRIPLA on an empty stomach.
- Swallow ATRIPLA with water.
- Taking ATRIPLA at bedtime may make some side effects less bothersome.
- Do not miss a dose of ATRIPLA. If you forget to take ATRIPLA, take the missed dose right away, unless it is almost time for your next dose. Do not double the next dose. Carry on with your regular dosing schedule. If you need help in planning the best times to take your medicine, ask your healthcare provider or pharmacist.
- If you believe you took more than the prescribed amount of ATRIPLA, contact your local poison control center or emergency room right away.
- Tell your healthcare provider if you start any new medicine or change how you take old ones. Your doses may need adjustment.
- When your ATRIPLA supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to ATRIPLA and become harder to treat.
- Your healthcare provider may want to do blood tests to check for certain side effects while you take ATRIPLA.

What should I avoid while taking ATRIPLA?

- **Women taking ATRIPLA should not become pregnant.** Serious birth defects have been seen in the babies of animals and women treated with efavirenz (a component of ATRIPLA) during pregnancy. It is not known whether efavirenz caused these defects. **Tell your healthcare provider right away if you are pregnant.** Also talk with your healthcare provider if you want to become pregnant.
- Women should not rely only on hormone-based birth control, such as pills, injections, or implants, because ATRIPLA may make these contraceptives ineffective. Women must use a reliable form of barrier contraception, such as a condom or diaphragm, even if they also use other methods of birth control.
- **Do not breast-feed if you are taking ATRIPLA.** The Centers for Disease Control and Prevention recommend that mothers with HIV not breast-feed because they can pass the HIV through their milk to the baby. Also, ATRIPLA may pass through breast milk and cause serious harm to the baby. Talk with your healthcare provider if you are breast-feeding. You should stop breast-feeding or may need to use a different medicine.
- Taking ATRIPLA (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg) with alcohol or other medicines causing similar side effects as ATRIPLA, such as drowsiness, may increase those side effects.
- Do not take any other medicines, including prescription and nonprescription medicines and herbal products, without checking with your healthcare provider.
- **Avoid doing things that can spread HIV infection** since ATRIPLA does not stop you from passing the HIV infection to others.

What are the possible side effects of ATRIPLA?

ATRIPLA may cause the following serious side effects:

- **Lactic acidosis** (buildup of an acid in the blood). Lactic acidosis can be a medical emergency and may need to be treated in the hospital. **Call your healthcare provider right away if you get signs of lactic acidosis.** (See "What is the most important information I should know about ATRIPLA?")
- **Serious liver problems (hepatotoxicity),** with liver enlargement (hepatomegaly) and fat in the liver (steatosis). Call your healthcare provider right away if you get any signs of liver problems. (See "What is the most important information I should know about ATRIPLA?")
- **"Flare-ups" of Hepatitis B Virus (HBV) infection,** in which the disease suddenly returns in a worse way than before, can occur if you have HBV and you stop taking ATRIPLA. Your healthcare provider will monitor your condition for several months after stopping ATRIPLA if you have both HIV and HBV infection and may recommend treatment for your HBV.
- **Serious psychiatric problems.** A small number of patients may experience severe depression, strange thoughts, or angry behavior while taking ATRIPLA. Some patients have thoughts of suicide and a few have actually committed suicide. These problems may occur more often in patients who have had mental illness. Contact your healthcare provider right away if you think you are having these psychiatric symptoms, so your healthcare provider can decide if you should continue to take ATRIPLA.
- **Kidney problems.** If you have had kidney problems in the past or take other medicines that can cause kidney problems, your healthcare provider should do regular blood tests to check your kidneys.
- **Changes in bone mineral density (thinning bones).** It is not known whether long-term use of ATRIPLA will cause damage to your bones. If you have had bone problems in the past, your healthcare provider may need to do tests to check your bone mineral density or may prescribe medicines to help your bone mineral density.

Common side effects:

Patients may have dizziness, headache, trouble sleeping, drowsiness, trouble concentrating, and/or unusual dreams during treatment with ATRIPLA. These side effects may be reduced if you take ATRIPLA at bedtime on an empty stomach. They also tend to go away after you have taken the medicine for a few weeks. If you have these common side effects, such as dizziness, it does not mean that you will also have serious psychiatric problems, such as severe depression, strange thoughts, or angry behavior. Tell your healthcare provider right away if any of these side effects continue or if they bother you. It is possible that these symptoms may be more severe if ATRIPLA is used with alcohol or mood altering (street) drugs.

If you are dizzy, have trouble concentrating, or are drowsy, avoid activities that may be dangerous, such as driving or operating machinery.

Rash may be common. Rashes usually go away without any change in treatment. In a small number of patients, rash may be serious. If you develop a rash, call your healthcare provider right away.

Other common side effects include tiredness, upset stomach, vomiting, gas, and diarrhea.

Other possible side effects with ATRIPLA include:

- Changes in body fat. Changes in body fat develop in some patients taking anti-HIV medicine. These changes may include an increased amount of fat in the upper back and neck ("buffalo hump"), in the breasts, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these fat changes are not known.
- Skin discoloration (small spots or freckles) may also happen with ATRIPLA.

Tell your healthcare provider or pharmacist if you notice any side effects while taking ATRIPLA.

Contact your healthcare provider before stopping ATRIPLA because of side effects or for any other reason.

This is not a complete list of side effects possible with ATRIPLA. Ask your healthcare provider or pharmacist for a more complete list of side effects of ATRIPLA and all the medicines you will take.

How do I store ATRIPLA?

- **Keep ATRIPLA and all other medicines out of reach of children.**
- Store ATRIPLA at room temperature 77 °F (25 °C).
- Keep ATRIPLA in its original container and keep the container tightly closed.
- Do not keep medicine that is out of date or that you no longer need. If you throw any medicines away make sure that children will not find them.

General information about ATRIPLA:

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use ATRIPLA for a condition for which it was not prescribed. Do not give ATRIPLA to other people, even if they have the same symptoms you have. It may harm them.

This leaflet summarizes the most important information about ATRIPLA. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about ATRIPLA that is written for health professionals.

Do not use ATRIPLA if the seal over bottle opening is broken or missing.

What are the ingredients of ATRIPLA?

Active Ingredients: efavirenz, emtricitabine, and tenofovir disoproxil fumarate

Inactive Ingredients: croscarmellose sodium, hydroxypropyl cellulose, microcrystalline cellulose, magnesium stearate, sodium lauryl sulfate. The film coating contains black iron oxide, polyethylene glycol, polyvinyl alcohol, red iron oxide, talc, and titanium dioxide.

℞ **ONLY**

July 2006

Bristol-Myers Squibb GILEAD

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Articles

On the cover:

Dean Triantafillo, longterm survivor.

Photo by ©Russell McGonagle. See story on page 18.

Distribution of *Positively Aware* is supported in part through grants from GlaxoSmithKline and Abbott Laboratories.

A model, photograph, or author's HIV status should not be assumed based on their appearance in *Positively Aware.*

You can view these (and other stories from previous issues) online at **http://www.tpan.com**

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Programs and Meetings at TPAN

- Support Groups
- Rapid HIV Testing
- Reiki and Massage
- Needle Exchange Program
- Individual Counseling
- Peer Support Network/Buddy Program
- Speakers Bureau
- Access Medical Clinic at TPAN
- PULSE, an HIV-positive Weekly Social
- TEAM (Treatment Education Advocacy Management)
- Positively Wired—A Free Basic Computer Skills Workshop

For detailed descriptions of programs, including days, times and locations, go to http://www.tpan.com/client_services/clientservices.shtml or visit www.tpan.com and click on Client Services, or call (773) 989-9400

TPAN Events Calendar

TPAN Events Calendar

- Educational Forums and Trainings
- Special Events

For detailed descriptions of upcoming TPAN events go to http://www.tpan.com/events/events.shtml or visit www.tpan.com and click on Events, or call (773) 989-9400

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Rescue me

Salvage. Rescue. Treatment experience. You may have read or heard one of these terms recently, but what do really they mean?

Salvage therapy

Salvage or rescue therapy in HIV usually refers to someone who is experiencing treatment failure—a suboptimal response to therapy—and who no longer has any effective treatment options available. There can be many reasons for treatment failure, including drug resistance, non-adherence, drug side effects, lack of a potent regimen, and pharmacokinetics (what your body does to the drug). But once the treatment fails, your chances for clinical progression, or developing more advanced HIV disease, increase—especially if your CD4 count is very low. Remember, though, that if this happens, you're not failing your treatment—your treatment is failing you!

Treatment experience

When I hear the term treatment-experienced, it always makes me think of a person who has gained great wisdom over the years when it comes to their own HIV treatment—but we know that this isn't always the case! All it really means is that it's not your first regimen.

In managing treatment-experienced patients, the Department of Health and Human Services (DHHS) Treatment Guidelines recommend evaluating antiretroviral treatment failure, including assessing the severity of HIV disease, treatment history, and results of drug resistance testing while determining the level of prior treatment exposure and resistance—limited, intermediate, or extensive. The goal of treatment is to achieve maximal virologic suppression, and when viral suppression is difficult or impossible to achieve with currently available drugs, to preserve the immune system and prevent clinical progression. Above all, it's crucial to obtain expert medical advice.

It's important to bear in mind that most people *benefit* from antiretroviral therapy (ART), and the majority of those on an ART regimen can keep their viral load undetectable for 3–6 years, or even longer. Some factors which have *not* been associated with treatment failure include gender, race, pregnancy, and a history of past substance use.

A little history

So what does all of this mean to you? Well, for starters, arm yourself with knowledge! Do your research, study the Guidelines, plot out your treatment history, and then assess, along with your provider, where you fall on the spectrum of HIV treatment. Here's mine as an example:

- **November 1989:** Started AZT (zidovudine, Retrovir) 600 mg per day; CD4 count under 500
- **September 1994:** Switched to d4T (stavudine, Zerit) 40 mg twice daily because of CD4 count of 177
- **May 1995:** Switched to 3TC (lamivudine, Epivir) 150 mg + d4T twice daily
- **September 1996:** Switched to 3TC + AZT 300 mg + nevirapine (Viramune) 200 mg twice daily after receiving first viral load test—viral load was 20,800; CD4 count 324
- **November 1996:** Viral load increased to 40,500; switched to 3TC + AZT + indinavir (Crixivan)
- **August 1998:** Developed kidney stones; switched to 3TC + AZT + nelfinavir (Viracept)
- **June 2001:** Due to viral load of 14,600 and the results of a genotypic resistance test, switched to Kaletra (lopinavir/ritonavir) + efavirenz (Sustiva, Stocrin); have had great success with this regimen—viral load remains undetectable and CD4 count hovers between 700 and 800

I probably would fall somewhere in the "intermediate" level of treatment-experience and resistance. I'm not considered to be on salvage therapy since my current regimen is working and my immune system relatively intact. However, if I were to develop resistance to the drugs that I'm currently on I could be in big trouble, potentially knocking out one or two powerful classes of drugs at the same time. New drugs coming to market this year makes this trouble unlikely. Then too, the side effects of this regimen, increased cholesterol and triglycerides, may soon be catching up with me. Luckily there might be other options that will be just as effective, and with fewer lipid effects.

The new treatment paradigm?

Today there are many new therapies that are or may soon become available, including: newer protease inhibitors and second generation non-nukes for people with multiple resistance mutations; and entire new classes of drugs, including *two* integrase inhibitors, Merck's MK-0518 and Gilead's GS-9137, as well as Pfizer's entry inhibitor maraviroc. How well these new drugs will work, and for how long, especially for those who are in need salvage of therapy, remains to be seen.

Finally I hear this question being asked: Is there no longer a need for salvage therapy? While it is true that the need may not be as pressing as it was 10 or 20 years ago, it still exists. Unfortunately as long as there are those who need new medications in order to construct a viable regimen, and until we learn how to develop therapies that are easier to take, have fewer side effects, are more potent and tolerable, and that we are less likely to develop resistance to—we'll be in need of rescue.

Take care of yourself, and each other.

Jeff Berry
Editor
publications@tpan.com

To learn more about salvage therapy visit www.aidsinfonet.org, www.TheBody.com, and www.aidsinfo.nih.gov.

Photo © Russell McGonagle

Readers Forum

Positively Aware will treat all communications (letters, faxes, e-mail, etc.) as letters to the editor unless otherwise instructed. We reserve the right to edit for length, style or clarity. Please advise if we can use your name and city.

Write to: *Positively Aware*,
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Chicago, IL 60640
Fax: (773) 989–9494
E-mail: readersforum@tpan.com

2007 Drug Guide

Positively Aware inadvertently left out Associate Editor Enid Vázquez's name from the credit for updating this year's drug guide. Our sincere apologies to her for the oversight.

First off, I want to thank you so much for the Positively Aware Eleventh Annual HIV Drug Guide [January/February issue]. It helps our staff explain the different HIV treatment options to our patients. We usually order extra copies to hand out to the patients throughout the year. Our staff and patients eagerly await each issue of your fine magazine.

I was also intrigued by the artwork on the cover of the Jan/Feb issue and was wondering if you could tell me anything about the artist and the artwork on and throughout the magazine.

Thanks
Gary Dyak, UCSD AVRC, San Diego

Editor's note: Our wonderfully talented graphic designer, Russell McGonagle, has been with us now for the last ten and a half years. To order additional copies of the Drug Guide, e-mail us at distribution@tpan.com.

HIV morning-after pill

I was surprised to read about a new trend among partygoers to use tenofovir (Viread) as a preventive treatment before engaging in risky sexual behaviors. From *OUT* (January 2007), "And AIDS experts say there's a growing number of HIV-negative men who take a single dose of tenofovir before a night of partying, hookups, and possibly unprotected sex in the hopes that it will keep them from contracting HIV."

Using the principles of harm reduction, it makes sense for doctors to prescribe tenofovir for patients who admit they engage in unsafe sex and don't plan to stop doing this. Again from the *OUT* article, "It's not something I routinely offer to all my HIV-negative patients," Mills explains. "But what I'm seeing lately is that many of my patients are having more risky sex, whether it's due to condom fatigue or the use of crystal meth, or that they have a partner who's positive, or for a lot of other reasons."

What scares me most about this strategy is that there's not much proof that Viread works or to what extent it is effective. Assuming that it is mostly effective, I suppose it would decrease the spread of HIV among gay men, but also encourages reckless behavior and gives little incentive for prevention education programs to be developed and funded. I guess if the physician/patient relationship is good and honest, then an ethical physician would only recommend this strategy to patients who refuse to take other precautions.

On a positive note, this option places the responsibility for health and safety into the hands of the individual rather than some trends where HIV-negative men assume anyone who is HIV-positive would care about their health and assume the responsibility for minimal risk to the HIV-negative partner. Unfortunately, that rarely happens, for many HIV-positive men experience emotional trauma ranging from denial to anger to revenge to apathy, and often can be reckless when it comes to substance abuse and sexual practices.

In my opinion, the answer is an instant HIV test that would be marketed and sold to HIV-negative men for use. Making a pre-sexual encounter HIV test a normal event may ruin the moment for men who have something to worry about, but could not be much worse than stopping to talk about and/or use condoms. Condoms still have their place and purpose in prevention of many other STDs, but the instant HIV test would give the HIV-negative man the option of screening their sexual partners, something that in time could become a wise and responsible thing to do. At the very least, it would provoke a conversation about sexual history, etc… and may even prompt the two individuals to choose other ways to enjoy each others' company.

I'm sure this debate will be heated and my opinion is just that, an opinion.

Joe Doedtman, Chicago, via the Internet

Atripla

Could you please send me the 2007 HIV drug guide? I am HIV-positive since March 1983 and in my final year of a seven year prison sentence. I continue to be grateful for all the educational materials I have gotten from *Positively Aware* since being a prisoner. I am currently on Atripla and I've got to tell you, this one pill a day combo sure beats the handful of combos I've taken … ddI, ddC, AZT, … d4T, 3TC … I've been on so many. But since 2000 I have had 500 plus T-cells and less than 400 viral load. Florida now uses a different test and I'm undetectable, less than 50 copies.

Name withheld, Indiantown, FL.

Nutrition

What a great article! ["Can It Get Any Better Than This?" by registered dietician Charlie Smigelski, Fall 2006 Special Issue]. Thanks for the clear, and, dare I say, digestible information.

John David Forsgren, via the Internet

Rap

Keeping up to date is a personal goal of mine, and information like that provided in *Positively Aware* will help me to continue to be informed. I contracted HIV/AIDS in 2000 at the age of 54 and am doing quite well, but want to work with others in my neighborhood to get prevention messages out to them. One program that I hope will be successful is a series of Public Service Announcements written and performed by

MARAVIROC Expanded Access Program

ASK YOUR DOCTOR IF THIS PROGRAM IS RIGHT FOR YOU

If you are HIV-positive and meet the criteria, and you and your doctor agree that it is appropriate, your doctor can enroll you in a research study, the Expanded Access Program (EAP) for maraviroc. Maraviroc is a new investigational HIV drug now being studied.

What is an EAP?

EAPs help people with limited or nonexistent treatment options get access to drugs not approved by the FDA.

Who can take part?

You may be able to join the maraviroc EAP if:

- You are at least 16 years of age (or minimum adult age as determined by local regulatory authorities or as dictated by local law)
- You are treatment-experienced
- You require maraviroc as a study treatment due to limited or nonexistent treatment options as determined by your doctor
- You have an HIV-1 RNA 1000 or more copies/mL
- You are a woman of child-bearing potential, your urine pregnancy test must be negative prior to the first dose of study medication

Other entry requirements will also need to be met.

How can the maraviroc EAP potentially help me?

If you qualify, this EAP can:

- Give you another treatment option where there are limited or no other options available because of resistance or intolerance of all currently approved HIV medications
- The study will continue for a period of ninety (90) days after commercial availability of the study drug or until Pfizer discontinues the study

What should I do if I am interested in enrolling in the maraviroc EAP?

If you are interested, talk to your doctor. If your doctor thinks you may be right for the EAP, he or she should visit:

www.maravirocEAP.com

The safety and effectiveness of maraviroc are not established. Maraviroc does not cure HIV. It does not stop you from giving HIV to others.

The health information contained herein is provided for educational purposes only and is not intended to replace discussions with a health care provider. All decisions regarding patient care must be made with a health care provider, considering the unique characteristics of patients.

MV276465I

February 2007

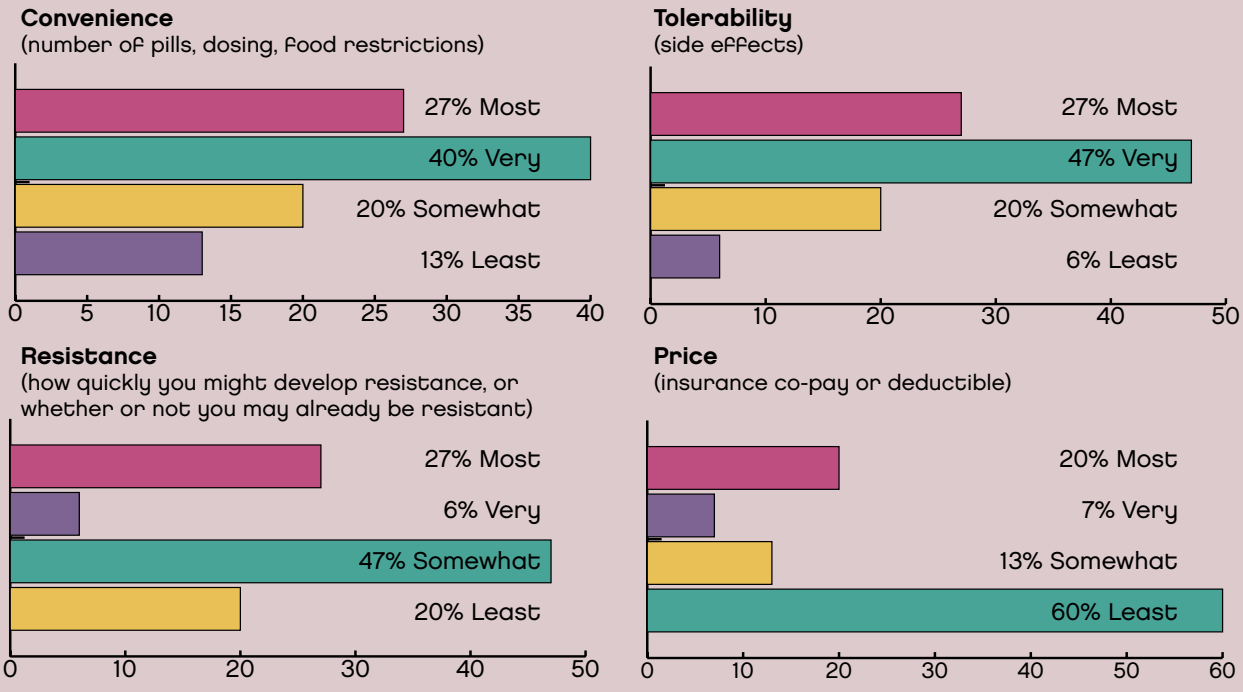
a young rap artist. We are in the process of developing the content and will go into production soon. A local organization, Tremendous Inc., has agreed to assist us in this venture. They have a full production studio and the necessary supporting services. Tremendous Inc. was formed by a local TV anchor person, Colleen Needles.

Jerry Clark, Founder & Chief Executive, WE CARE Minnesota, Saint Paul

Editor's note: The Chicago Black Gay Men's Caucus has produced a music video "I Know. Do You Know?" with lead vocals provided by Positively Aware *Associate Editor Keith R. Green. Visit www.lovethybrotha.com*

January / February 2007 PA Online Poll Results

What matters to you most when choosing an effective HIV therapy?



January / February 2007 PA Online Poll comments

- I have been pos for 10 years but am not on any meds yet and hope to stay that way for as long as possible.
- I have been on most all of the drugs available at one time or another. I have had CD4's at below 50 and am currently near 400! I am currently on Atripla which has been the easiest drug thus far. I have been lucky to have had insurance to pay my costs.

March / April 2007 PA Online Poll

How do you pay for your HIV medications?

ADAP (AIDS Drug Assistance Program)
Medicare
Medicaid
Private Insurance
Out of pocket
Other

Give your answer at www.tpan.com

by Enid Vázquez

Circumcision

The risk of getting infected with HIV decreased by half with the use of circumcision in NIAID research with 4,996 Ugandan men and 2,784 Kenyan men. "Many studies have suggested that male circumcision plays a role in protecting against HIV acquisition," Anthony S. Fauci, M.D., director of NIAID (National Institute of Allergy and Infectious Disease), said in a press release. "We now have confirmation—from large, carefully controlled, randomized clinical trials—showing definitively that medically performed circumcision can significantly lower the risk of adult males contracting HIV through heterosexual intercourse." Because the results clearly favored circumcision, NIAID stopped the research early and will offer circumcision to all men enrolled in the study. A French study in South Africa had previously shown that circumcision decreases the risk of infection. That study showed a 60% reduction in risk. Research has also found that the foreskin is rich in a type of cell that is very vulnerable to the virus. NIAID noted that the use of condoms and safer sex counseling is still important to slowing the epidemic. The World Health Organization (WHO) agreed with that concept in a statement, "emphasizing" that circumcision is not the complete answer. WHO said that it would look into the use of circumcision, but among its concerns, WHO noted that "the ideal and well-resourced conditions of a randomized trial" are not always available to men around the globe, including sanitary conditions. The epidemic in sub-Saharan Africa is driven primarily by heterosexual contact, and WHO noted that the rate of circumcision there is low. For extensive information on circumcision and HIV, visit www.aidsvaccineclearinghouse.org.

Prisons and HIV

An article in the January 11 issue of the prestigious *New England Journal of Medicine* explored HIV prevention in prisons. Author Susan Okie, M.D., noted that the World Health Organization (WHO) and UNAIDS (a program of the United Nations) have for more than 10 years recommended condoms in prisons. The agencies also recommend drug treatment, methadone, and bleach for cleaning injection supplies, plus having syringe exchange be considered. But the U.S. rarely makes those resources available to prisoners. Dr. Okie reported that in terms of harm reduction:

- prisons in several Western European countries and in Australia, Canada, Kyrgyzstan, Belarus, Moldova, Indonesia, and Iran have adopted some or all of these recommendations
- clean needles and syringes are available in approximately 50 prisons in eight countries
- evaluations of such programs in Switzerland, Spain, and Germany found no increase in drug use, a dramatic decrease in needle sharing, no new cases of infection with HIV or hepatitis B or C, and no reported instances of needles being used as weapons
- condoms are provided on a limited basis in two state prison systems in the U.S. (Vermont and Mississippi) and five county jail systems (New York, Philadelphia, San Francisco, Los Angeles, and Washington, D.C.)
- methadone maintenance programs are even more rare, available in a few jails and prisons, including those in New York City, Albuquerque, and San Juan, Puerto Rico
- no U.S. prison has provided a needle-exchange program

Dr. Okie also reported that:

- there were more than 2.2 million U.S. prisoners at the end of 2005, a record high
- drug-related offenses were a major reason for the increase in prisoners, responsible for half of the new numbers between 1995 and 2003
- more than half of all inmates had a mental health problem in 2005, and Dr. Okie wrote that "doctors who treat prisoners say that many have used illicit drugs as self-medication for untreated mental disorders"

As far as HIV goes:

- in 2004, 1.8% of prison inmates were HIV-positive, more than four times the estimated rate in the general population
- the rate of confirmed AIDS cases was also substantially higher
- it has been estimated that each year, about 25% (one out of four) of all HIV-positive persons in the U.S. spend time in a correctional facility, as do 33% of persons with hepatitis C and 40% of those with active TB
- between 1988—when the Georgia Department of Corrections began mandatory HIV testing of all inmates on entry to prison and voluntary testing thereafter—and 2005, HIV occurred in 88 male inmates in Georgia prisons; transmission resulted from men having sex with other men or getting a tattoo
- in another study in a southeastern state, HIV transmission while in prison was documented in 33 of 5,265 male inmates (0.63%)

"U.S. prison populations have higher rates of mental illness and violence than their European counterparts, which, some researchers argue, might make providing needles more dangerous," Dr. Okie writes. "And some believe that whereas European prison officials tend to be pragmatic [practical], many U.S. officials adopt a 'just deserts' philosophy, viewing infections as the consequences of breaking prison rules."

Photo © Russell McGonagle


He knows he has HIV. He doesn't know
his HIV puts him at risk for kidney disease.
Ask your doctor about your risk factors and the impact
that HIV and its treatment may have on your kidneys.

There's Nothing Routine About HIV

CDC's recommendations for HIV testing

by Matt Sharp

I was recently invited to a meeting in Washington, D.C. that brought together federal policy makers from the CDC, HIV researchers, care providers, and community members from all over the country to discuss the new CDC recommendations for routine HIV testing. The meeting was meant to be influential, with a long list of AIDS divas in attendance such as Anthony Fauci, Mathilde Krim, John Bartlett, and Phill Wilson. It was an eye opening attempt to lay out all the concerns about implementation of the recommendations.

A bit of a background: You've most likely heard HIV testing is now recommended everywhere that medical care is provided. It was first called for by Tom Frieden, the alarmist New York City Health Commissioner. That apparently was the spark that ignited the CDC to make its testing recommendations. And *voila*… a national policy became reality.

Routine HIV testing may be a good thing, but I left this meeting realizing there are many flaws and pitfalls in implementing this huge policy sea change. Every time the U.S. government dictates health policy, the system is not prepared for it. I chalk it up to another inadequate government plan, not unlike the Iraq invasion and occupation. There may just not be enough *troops* to perform all these HIV tests. I was frustrated once again at policy recommendations thrust into the arena that had not been thoroughly thought out with all the game players.

They *estimate* 250,000 people are HIV-positive in the U.S. and don't know it. Most people agree that there is a need to test all those "dissenters" of unknown status out there infecting everyone. But that is where the accord ends. Community members and providers worry that there will be a problem linking so many people into care once they test positive, and the legal and economic concerns are immense. But policy makers simply urge identifying high-risk individuals so they won't continue to fuel the epidemic.

One thing I kept thinking as a person living with HIV is that there is nothing at all "routine" about HIV. We're not talking about something as everyday as cholesterol screening. To call it routine is to deny the reality of a stigmatizing and deadly sexually transmitted disease where treatments are expensive and not accessible to everyone who's positive. Even today people are dying while on ADAP waiting lists. Yes, good treatments abound, but this country still hasn't solved the issue of exorbitant drug costs and barriers to drug access.

And hello, there still is no cure for HIV! It's still considered incurable if not manageable. So even though testing everyone and their mother is noble, it's not putting a realistic face on dealing with a chronic manageable life with AIDS.

Giving people positive test results is also certainly not routine. Those of you who are HIV-positive might think back to the time you were tested and remember how it felt. It wasn't an easy decision for most of us. Now the plan is to do away with or reduce any counseling, pre or post. There will simply be a condition to "opt out" of the test. That does makes it a bit less compulsory, but if you sign on the dotted line you are virtually left to the conditions of the site that tests you. There is no mandate for counseling and you may get a result without any support or referrals. Talk about taking a giant leap backwards!

It is also curious that this testing offensive coincides with the process of changing mandatory names reporting laws in many states, including here in Illinois. According to the CDC, all states have adopted some system or plan for collecting the names of people with HIV and AIDS. Some 15 years ago mandatory names reporting was like a scarlet letter to many people stigmatized by society because of their HIV status, sexuality, and race. There was a huge mobilization of the AIDS community to demand that testing be anonymous. A compromise was made and both confidential and anonymous testing were offered and the names of people with AIDS were all that were reported. Today, the names of HIV-positive individuals will be reported, but until we address HIV stigma that still exists, people will be wary of testing and disclosing their serostatus. Call me paranoid but I find this juxtaposition of routine testing and names reporting creepy.

And what about prevention? The policy makers contend that testing everyone will improve safer sex practices and thus reduce HIV transmission. Again, there is no strategy in place to counsel and teach those who test negative about ways to *stay* negative. There is no institutional strategy or the resources to pay for it. It's a bit cart-before-the-horse.

The bottom line with this new policy from my point of view is the consideration of *human rights*. On paper HIV testing will help to stem the epidemic. But until inquiring minds come together to focus on civil and human rights and strategize about the very best way to implement this policy, it is set up to fail.

Let's not march on with a George Bush *"Mission Accomplished"* testing policy until all the *t's* are crossed and *i's* are dotted.

Photo © Russell McGonagle

There's a new reason to ask about

REYATAZ®
(atazanavir sulfate) 200 mg/300 mg capsules

Now it's the only one pill, once-a-day protease inhibitor (PI) as part of HIV combination therapy.*

*Single pill REYATAZ is for patients who have taken anti-HIV medicines before. It must be taken with ritonavir once daily in HIV combination therapy.

REYATAZ does not cure HIV, a serious disease, or help prevent passing HIV to others.

REYATAZ, a protease inhibitor (PI) taken in HIV combination therapy:

- **Can help raise your T-cells**
- **Can help lower your viral load to undetectable**†
- **Low chance of diarrhea** (shown in clinical trials)‡

† Undetectable is defined as a viral load of less than 400 or 50 copies/mL (depending on the test used).
‡ REYATAZ in combination therapy had a 1-3% rate of moderate-to-severe diarrhea.

one pill, once-a-day in combination therapy*

REYATAZ®
(atazanavir sulfate) 200 mg/300 mg capsules

ASK YOUR DOCTOR if REYATAZ, in HIV combination therapy, can help you fight HIV your way.

IMPORTANT INFORMATION ABOUT REYATAZ (atazanavir sulfate)

INDICATION: REYATAZ (atazanavir sulfate) is a prescription medicine used in combination with other medicines to treat people who are infected with the human immunodeficiency virus (HIV). REYATAZ has been studied in 48-week trials in both patients who have taken or have never taken anti-HIV medicines.

REYATAZ does not cure HIV or help prevent passing HIV to others.

IMPORTANT SAFETY INFORMATION:

Do not take REYATAZ if you are taking the following medicines: ergot medicines, Versed®, Halcion®, Orap®, Propulsid®, Camptosar®, Crixivan®, Mevacor®, Zocor®, rifampin, St. John's wort, AcipHex®, Nexium®, Prevacid®, Prilosec®, or Protonix®. Do not use Viagra®, Levitra®, Cialis®, Vfend®, Advair®, Flonase®, or Flovent® while you are taking REYATAZ without first speaking with your healthcare provider. **This list of medicines is not complete. Discuss all prescription and non-prescription medicines, vitamin and herbal supplements, or other health preparations you are taking or plan to take with your healthcare provider.**

Tell your healthcare provider right away if you have any side effects or conditions, including the following:

- **A change in the way your heart beats** may occur and could be a symptom of a heart problem.
- **Diabetes and high blood sugar** may occur in patients taking protease inhibitor medicines like REYATAZ (atazanavir sulfate).
- **Yellowing of the skin and/or eyes** may occur due to increases in bilirubin levels in the blood (bilirubin is made by the liver).
- **Rash** (redness and itching) sometimes occurs in patients taking REYATAZ, most often in the first few weeks after the medicine is started, and usually goes away within two weeks with no change in treatment.
- **If you have liver disease,** including hepatitis B or C, your liver disease may get worse when you take anti-HIV medicines like REYATAZ (atazanavir sulfate).
- **Some patients with hemophilia** have increased bleeding problems with protease inhibitor medicines like REYATAZ.

Changes in body fat have been seen in some patients taking anti-HIV medicines. The cause and long-term effects are not known at this time.

Other side effects of REYATAZ taken with other anti-HIV medicines include: nausea, headache, stomach pain, vomiting, diarrhea, depression, fever, dizziness, trouble sleeping, numbness, and tingling or burning of hands or feet.

You should take REYATAZ once daily with food (a meal or snack). You should take REYATAZ and your other anti-HIV medicines exactly as instructed by your healthcare provider.

Please see Important Patient Information about REYATAZ on the next page.

Bristol-Myers Squibb

PATIENT INFORMATION

℞ ONLY

REYATAZ® (RAY-ah-taz)

(generic name = **atazanavir sulfate**) **Capsules**

ALERT: Find out about medicines that should NOT be taken with REYATAZ (atazanavir sulfate). Read the section "What important information should I know about taking REYATAZ with other medicines?"

Read the Patient Information that comes with REYATAZ before you start using it and each time you get a refill. There may be new information. This leaflet provides a summary about REYATAZ and does not include everything there is to know about your medicine. This information does not take the place of talking with your healthcare provider about your medical condition or treatment.

What is REYATAZ?

REYATAZ is a prescription medicine used with other anti-HIV medicines to treat people who are infected with the human immunodeficiency virus (HIV). HIV is the virus that causes acquired immune deficiency syndrome (AIDS). REYATAZ is a type of anti-HIV medicine called a protease inhibitor. HIV infection destroys CD4+ (T) cells, which are important to the immune system. The immune system helps fight infection. After a large number of (T) cells are destroyed, AIDS develops. REYATAZ helps to block HIV protease, an enzyme that is needed for the HIV virus to multiply. REYATAZ may lower the amount of HIV in your blood, help your body keep its supply of CD4+ (T) cells, and reduce the risk of death and illness associated with HIV.

Does REYATAZ cure HIV or AIDS?

REYATAZ does not cure HIV infection or AIDS. At present there is no cure for HIV infection. People taking REYATAZ may still get opportunistic infections or other conditions that happen with HIV infection. Opportunistic infections are infections that develop because the immune system is weak. Some of these conditions are pneumonia, herpes virus infections, and *Mycobacterium avium* complex (MAC) infections. **It is very important that you see your healthcare provider regularly while taking REYATAZ.**

REYATAZ does not lower your chance of passing HIV to other people through sexual contact, sharing needles, or being exposed to your blood. For your health and the health of others, it is important to always practice safer sex by using a latex or polyurethane condom or other barrier to lower the chance of sexual contact with semen, vaginal secretions, or blood. Never use or share dirty needles.

Who should not take REYATAZ?

Do not take REYATAZ if you:

- **are taking certain medicines**. (See "What important information should I know about taking REYATAZ with other medicines?") Serious life-threatening side effects or death may happen. Before you take REYATAZ, tell your healthcare provider about all medicines you are taking or planning to take. These include other prescription and nonprescription medicines, vitamins, and herbal supplements.
- **are allergic to REYATAZ or to any of its ingredients.** The active ingredient is atazanavir sulfate. See the end of this leaflet for a complete list of ingredients in REYATAZ. Tell your healthcare provider if you think you have had an allergic reaction to any of these ingredients.

What should I tell my healthcare provider before I take REYATAZ?

Tell your healthcare provider:

- **If you are pregnant or planning to become pregnant**. It is not known if REYATAZ can harm your unborn baby. Pregnant women have experienced serious side effects when taking REYATAZ with other HIV medicines called nucleoside analogues. You and your healthcare provider will need to decide if REYATAZ is right for you. If you use REYATAZ while you are pregnant, talk to your healthcare provider about the Antiretroviral Pregnancy Registry.
- **If you are breast-feeding**. You should not breast-feed if you are HIV-positive because of the chance of passing HIV to your baby. Also, it is not known if REYATAZ can pass into your breast milk and if it can harm your baby. If you are a woman who has or will have a baby, talk with your healthcare provider about the best way to feed your baby.
- **If you have liver problems or are infected with the hepatitis B or C virus**. See "What are the possible side effects of REYATAZ?"
- **If you have diabetes**. See "What are the possible side effects of REYATAZ?"
- **If you have hemophilia**. See "What are the possible side effects of REYATAZ?"
- **About all the medicines you take** including prescription and nonprescription medicines, vitamins, and herbal supplements. Keep a list of your medicines with you to show your healthcare provider. For more information, see "What important information should I know about taking REYATAZ with other medicines?" and "Who should not take REYATAZ?" Some medicines can cause serious side effects if taken with REYATAZ.

How should I take REYATAZ?

- **Take REYATAZ once every day exactly as instructed by your healthcare provider**. Your healthcare provider will prescribe the amount of REYATAZ that is right for you.
  - For adults who have never taken anti-HIV medicines before, the usual dose is 400 mg (two 200-mg capsules) once daily taken with food.
  - For adults who have taken anti-HIV medicines in the past, the usual dose is 300 mg (one 300-mg capsule or two 150-mg capsules) plus 100 mg of NORVIR® (ritonavir) once daily taken with food.

  Your dose will depend on your liver function and on the other anti-HIV medicines that you are taking. REYATAZ is always used with other anti-HIV medicines. If you are taking REYATAZ with SUSTIVA® (efavirenz) or with VIREAD® (tenofovir disoproxil fumarate), you should also be taking NORVIR® (ritonavir).
- **Always take REYATAZ with food** (a meal or snack) to help it work better. Swallow the capsules whole. **Do not open the capsules**. Take REYATAZ at the same time each day.
- **If you are taking antacids or didanosine (VIDEX® or VIDEX® EC),** take REYATAZ 2 hours before or 1 hour after these medicines.
- **If you are taking medicines for indigestion, heartburn, or ulcers such as AXID® (nizatidine), PEPCID AC® (famotidine), TAGAMET® (cimetidine), or ZANTAC® (ranitidine),** talk to your healthcare provider.
- **Do not change your dose or stop taking REYATAZ without first talking with your healthcare provider**. It is important to stay under a healthcare provider's care while taking REYATAZ.
- **When your supply of REYATAZ starts to run low**, get more from your healthcare provider or pharmacy. It is important not to run out of REYATAZ. The amount of HIV in your blood may increase if the medicine is stopped for even a short time.
- **If you miss a dose of REYATAZ**, take it as soon as possible and then take your next scheduled dose at its regular time. If, however, it is within 6 hours of your next dose, do not take the missed dose. Wait and take the next dose at the regular time. Do not double the next dose. **It is important that you do not miss any doses of REYATAZ or your other anti-HIV medicines**.
- **If you take more than the prescribed dose of REYATAZ**, call your healthcare provider or poison control center right away.

Can children take REYATAZ?

REYATAZ has not been fully studied in children under 16 years of age. REYATAZ should not be used in babies under the age of 3 months.

What are the possible side effects of REYATAZ?

The following list of side effects is **not** complete. Report any new or continuing symptoms to your healthcare provider. If you have questions about side effects, ask your healthcare provider. Your healthcare provider may be able to help you manage these side effects.

The following side effects have been reported with REYATAZ:

- **rash** (redness and itching) sometimes occurs in patients taking REYATAZ, most often in the first few weeks after the medicine is started. Rashes usually go away within 2 weeks with no change in treatment. Tell your healthcare provider if rash occurs.
- **yellowing of the skin or eyes**. These effects may be due to increases in bilirubin levels in the blood (bilirubin is made by the liver). Call your healthcare provider if your skin or the white part of your eyes turn yellow. Although these effects may not be damaging to your liver, skin, or eyes, it is important to tell your healthcare provider promptly if they occur.
- **a change in the way your heart beats (heart rhythm change)**. Call your healthcare provider right away if you get dizzy or lightheaded. These could be symptoms of a heart problem.
- **diabetes and high blood sugar (hyperglycemia)** sometimes happen in patients taking protease inhibitor medicines like REYATAZ. Some patients had diabetes before taking protease inhibitors while others did not. Some patients may need changes in their diabetes medicine.
- **if you have liver disease** including hepatitis B or C, your liver disease may get worse when you take anti-HIV medicines like REYATAZ (atazanavir sulfate).
- **some patients with hemophilia** have increased bleeding problems with protease inhibitors like REYATAZ.
- **changes in body fat**. These changes may include an increased amount of fat in the upper back and neck ("buffalo hump"), breast, and around the trunk. Loss of fat from the legs, arms, and face may also happen. The cause and long-term health effects of these conditions are not known at this time.

Other common side effects of REYATAZ taken with other anti-HIV medicines include nausea; headache; stomach pain; vomiting; diarrhea; depression; fever; dizziness; trouble sleeping; numbness, tingling, or burning of hands or feet; and muscle pain.

What important information should I know about taking REYATAZ with other medicines?

Do not take REYATAZ if you take the following medicines (not all brands may be listed; tell your healthcare provider about all the medicines you take). REYATAZ may cause serious, life-threatening side effects or death when used with these medicines.

- Ergot medicines: dihydroergotamine, ergonovine, ergotamine, and methylergonovine such as CAFERGOT®, MIGRANAL®, D.H.E. 45®, ergotrate maleate, METHERGINE®, and others (used for migraine headaches).
- HALCION® (triazolam, used for insomnia).
- VERSED® (midazolam, used for sedation).
- ORAP® (pimozide, used for Tourette's disorder).
- PROPULSID® (cisapride, used for certain stomach problems).

Do not take the following medicines with REYATAZ because of possible serious side effects:

- CAMPTOSAR® (irinotecan, used for cancer).
- CRIXIVAN® (indinavir, used for HIV infection). Both REYATAZ and CRIXIVAN sometimes cause increased levels of bilirubin in the blood.
- Cholesterol-lowering medicines MEVACOR® (lovastatin) or ZOCOR® (simvastatin).

Do not take the following medicines with REYATAZ because they may lower the amount of REYATAZ in your blood. This may lead to an increased HIV viral load. Resistance to REYATAZ or cross-resistance to other HIV medicines may develop:

- Rifampin (also known as RIMACTANE®, RIFADIN®, RIFATER®, or RIFAMATE®, used for tuberculosis).
- St. John's wort (*Hypericum perforatum*), an herbal product sold as a dietary supplement, or products containing St. John's wort.
- "Proton-pump inhibitors" used for indigestion, heartburn, or ulcers such as AcipHex® (rabeprazole), NEXIUM® (esomeprazole), PREVACID® (lansoprazole), PRILOSEC® (omeprazole), or PROTONIX® (pantoprazole).

Do not take the following medicine if you are taking REYATAZ and NORVIR® together.

- VFEND® (voriconazole).

The following medicines may require your healthcare provider to monitor your therapy more closely:

- CIALIS® (tadalafil), LEVITRA® (vardenafil), or VIAGRA® (sildenafil). REYATAZ may increase the chances of serious side effects that can happen with CIALIS, LEVITRA, or VIAGRA. Do not use CIALIS, LEVITRA, or VIAGRA while you are taking REYATAZ unless your healthcare provider tells you it is okay.
- LIPITOR® (atorvastatin). There is an increased chance of serious side effects if you take REYATAZ with this cholesterol-lowering medicine.
- Medicines for abnormal heart rhythm: CORDARONE® (amiodarone), lidocaine, quinidine (also known as CARDIOQUIN®, QUINIDEX®, and others).
- VASCOR® (bepridil, used for chest pain).
- COUMADIN® (warfarin).
- Tricyclic antidepressants such as ELAVIL® (amitriptyline), NORPRAMIN® (desipramine), SINEQUAN® (doxepin), SURMONTIL® (trimipramine), TOFRANIL® (imipramine), or VIVACTIL® (protriptyline).
- Medicines to prevent organ transplant rejection: SANDIMMUNE® or NEORAL® (cyclosporin), RAPAMUNE® (sirolimus), or PROGRAF® (tacrolimus).
- The antidepressant trazodone (DESYREL® and others).
- Fluticasone propionate (ADVAIR®, FLONASE®, FLOVENT®), given by nose or inhaled to treat allergic symptoms or asthma. Your doctor may choose not to keep you on fluticasone, especially if you are also taking NORVIR®.

The following medicines may require a change in the dose or dose schedule of either REYATAZ or the other medicine:

- FORTOVASE®, INVIRASE® (saquinavir).
- NORVIR® (ritonavir).
- SUSTIVA® (efavirenz).
- Antacids or buffered medicines.
- VIDEX® (didanosine).
- VIREAD® (tenofovir disoproxil fumarate).
- MYCOBUTIN® (rifabutin).
- Calcium channel blockers such as CARDIZEM® or TIAZAC® (diltiazem), COVERA-HS® or ISOPTIN SR® (verapamil), and others.
- BIAXIN® (clarithromycin).
- Medicines for indigestion, heartburn, or ulcers such as AXID® (nizatidine), PEPCID AC® (famotidine), TAGAMET® (cimetidine), or ZANTAC® (ranitidine).

Women who use birth control pills or "the patch" should choose a different kind of contraception. REYATAZ may affect the safety and effectiveness of birth control pills or the patch. Talk to your healthcare provider about choosing an effective contraceptive.

Remember:

1. **Know all the medicines you take.**
2. **Tell your healthcare provider about all the medicines you take.**
3. **Do not start a new medicine without talking to your healthcare provider.**

How should I store REYATAZ?

- Store REYATAZ Capsules at room temperature, 59° to 86° F (15° to 30° C). Do **not** store this medicine in a damp place such as a bathroom medicine cabinet or near the kitchen sink.
- Keep your medicine in a tightly closed container.
- Throw away REYATAZ when it is outdated or no longer needed by flushing it down the toilet or pouring it down the sink.

General information about REYATAZ

This medicine was prescribed for your particular condition. Do not use REYATAZ for another condition. Do not give REYATAZ to other people, even if they have the same symptoms you have. It may harm them. **Keep REYATAZ and all medicines out of the reach of children and pets**.

This summary does not include everything there is to know about REYATAZ. Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Remember no written summary can replace careful discussion with your healthcare provider. If you would like more information, talk with your healthcare provider or you can call 1-800-321-1335.

What are the ingredients in REYATAZ?

Active Ingredient: atazanavir sulfate

Inactive Ingredients: Crospovidone, lactose monohydrate (milk sugar), magnesium stearate, gelatin, FD&C Blue #2, titanium dioxide, black iron oxide, red iron oxide, and yellow iron oxide.

Bristol-Myers Squibb Company

Princeton, NJ 08543 USA

This Patient Information Leaflet has been approved by the U.S. Food and Drug Administration.

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Revised October 2006

Ask the HIV Specialist™

Dear AAHIVM HIV Specialist™:

I've been recently seeing AIDS/HIV flyers everywhere I turn, and I find myself constantly questioning my own recent experiences and freaking out. I had unprotected oral sex about 4–5 months ago with a woman who said she had been tested and was negative, but I can't be sure. And I've also been reading mixed reports about oral sex and virus transmission. What are the chances that she may or may not have passed something on to me?

Jamal

Dear Jamal:

Being "freaked out" about the possibility of having HIV is a common reaction, but the best way to put an end to it is by being tested for HIV. The test now can often be done as a rapid test with preliminary results in 20 minutes and can use an oral swab to make it easier to test than a blood test.

The CDC issued new recommendations in September 2006, that all patients between ages 13 and 64 be tested for HIV at least once, removing any stigma in requesting an HIV test from your doctor. The new recommendations also suggest yearly testing for anyone who uses IV drugs, has sex with more than one partner in a year, has a partner who has sex with other people, is a male who has sex with other males, or any person who exchanges sex for money or drugs.

Oral sex does have some risk for transmission of HIV, but much less than other sexual activity. The Department of Health and Human Services in January of 2005 estimated that insertive oral intercourse carried with it a chance of being infected of 5/100,000 exposures, compared to 500/100,000 exposures of receptive anal sex, so oral intercourse is 100 times less risky than receptive anal intercourse. There is still the possibility of getting HIV from oral sex.

Many people, when they first become infected with HIV, have an acute retroviral syndrome, which is like having a bad flu, consisting of fever, sore throat, rash, muscle aches and fatigue. Not everyone will have such a reaction, however, so the best way to know is to get an HIV test.

David Piontkowsky, JD, MD
Medical Director, Positive Health Clinic
Allegheny General Hospital
Pittsburgh, PA

Dear AAHIVM HIV Specialist™:

I have been HIV-positive since '93. I've been on Crixivan, Viramune and Combivir for my HIV treatment. The lipodystrophy is annoying and is beginning to be a serious focus for me. My T-cells are at about 400 and I have no detectable viral load. I read recently that if you get off the drugs causing the lipo it can reverse over time. I have asked my specialist if I can change regimens so I can go from "less belly to more butt" someday.

What questions do I need to ask my doctor to get him thinking my way? Can you recommend a regimen that has been effective with others that were on mine? I have CAD, diabetes type II and take drugs for cholesterol and triglycerides as well. Any good data you could supply would be greatly appreciated. I expect to make a renewed effort for change after the New Year begins.

Regards,
Rodney

Dear Rodney,

I understand your concern about your regimen and the resulting lipodystrophy. Many patients and physicians continue to have this discussion. Unfortunately, there is no simple answer. Your T-cells and HIV viral load are doing well on this regimen and resistance testing was unsuccessful due to insufficient virus. You also mention your diabetes, lipid abnormalities and coronary artery disease (CAD) without further defining the problem. It is likely, then, that you may have "metabolic syndrome," although you don't mention your weight or blood pressure.

Remember that switching therapies without resistance testing is not recommended generally, but may be acceptable if you have been on the same regimen since you started treatment. If you both decide to take a chance and change, changing from AZT to tenofovir may help with the lipodystrophy. Also, a low-fat, high-fiber diet combined with both cardiovascular and resistance exercise can also have a positive impact. Using rosiglitazone [Avandia] to treat your diabetes, and possibly using testosterone supplementation depending on your tests, each might have small positive and additive effects.

The good news is we can effectively treat the virus. We still do face some challenges in treating problems associated with HIV, and with some of the side effects of otherwise effective antiviral therapy. Good luck to you! Because of the space limitations of a magazine column, I would be happy to provide more detailed explanations on any of the above recommendations, as well as any references for them that you or your physician may wish to receive.

R.H. Keller, MD, MS, FACP, AAHIVS
Hollywood, Florida

The American Academy of HIV Medicine (AAHIVM) is an independent organization of physicians, nurse practitioners, physician assistants and others dedicated to advancing excellence in HIV care through the HIV Specialist™ credentialing program, advocacy work and continuing education opportunities. E-mail your questions to aahivm@tpan.com.

TALES OF SALVAGE

Three men tell their story in a new era of HIV treatment

by Enid Vázquez

photos by Russell McGonagle

A decade ago "Lazarus syndrome" was used to describe people coming back from near death with the use of new HIV drugs. It was perhaps the most powerful moment in the history of AIDS.

But only in the past year, Chicagoan Dean Triantafillo (pictured) had a Lazarus event of his own, again with new HIV drugs. More than one powerful new drug is finally here for longterm survivors like Triantafillo who are heavily drug-resistant to mix into an effective combination, and more are soon to come.

Today people with HIV who have never seen an undetectable viral load are reaching that holy grail of therapy. Somewhat quietly, doctors and advocates are discussing the possibility that the spirit of 1996 has been reborn.

Near zero T-cells

Triantafillo had close to zero T-cells for nine years, but his doctor didn't want to change his HIV medications.

"He had me on therapy that wasn't doing shit, saying, 'Let's not rock the boat.' I kept telling him: I'm getting more fatigued each day. I have diarrhea. I don't feel well." When he ended up bedridden, he finally decided to find a new doctor. A friend recommended Dr. Frank Palella at Northwestern University hospital.

But there wasn't much Dr. Palella could do—not right away.

"He kept telling me, 'Dean, hang in there. A year from now, some new drugs are going to come out that will be wonderful for you because you're so [drug] resistant.' And he turned my life around. He had Prezista waiting for me at Walgreens the day it was approved." That was June 23. The drug is one of the second-generation protease inhibitors, developed for people whose virus is resistant to the ones that came out 10 years ago and many of the ones since then.

With his new therapy of Prezista (boosted by Norvir) and Truvada, Triantafillo began to improve immediately. In six months, he went from 105 pounds to 155. He works out and feels great, with no side effects. His T-cell count is 255 and his viral load is undetectable. "My friends and family say it's a miracle."

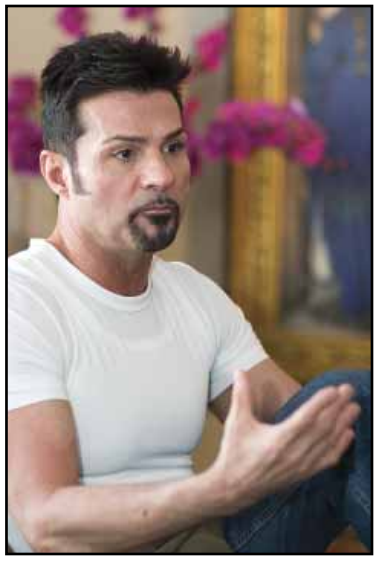
Triantafillo knows he's been infected since 1981 because that year, his partner came home with shingles, an opportunistic infection seen in people with a weakened immune system. Triantafillo had been with him for seven years. At that time, he was a patient at Chicago's Howard Brown Health Center, a clinic opened in the early 1980s for the gay and lesbian community. When Triantafillo developed symptoms of illness, a doctor there told him he was surely infected with this new disease. (An HIV test would not be available for another three years.)

"I was young and naïve. I had never been with anyone else and I trusted him completely," Triantafillo says of his partner, an airline pilot. "But it's okay. You learn how to take care of yourself."

He suffered through the Videx chalky tablets that had to be dispersed in water ("it tasted like cement") and the kidney stones of Crixivan. But he says he would have done almost anything for the chance to survive and to maintain some quality of life.

The Experiment

Bill Carter is a personal fitness trainer in Queens who says he can't list all the drug combinations he's taken because "there were so many." But since learning of his HIV infection 10 years ago, when he was very sick and came down with pneumonia, he's been continuously on therapy with anywhere from two weeks to two months off between drug regimens.



"I never wanted to stop because I was never undetectable," he says. "I figured if I stopped, my viral load would go up again."

Two years ago in March he entered a clinical study, taking Prezista (with Norvir booster), Fuzeon, and Truvada. Fuzeon, FDA-approved for advanced patients, is a potent drug that's generally reserved for that population because of its need for twice-daily injection.

Within three to four weeks he began to feel better. He could hold down his food and his diarrhea disappeared. Within six to eight

months his viral load went from a very high number in the 400,000 range down to undetectable. In that time, his weight went up 40 pounds to 185. The study staff said that his love of cooking helped him regain his health, as he focused on nutritionally sound eating. He also has had no problem with lipodystrophy—or body shape distortions due to fat problems, either thinning or increasing, as with abdominal distention. His study nurse said that anecdotally, the clinic staff finds that to be the case in people who have regular cardio workouts the way he does.

He says he loves his job, and takes care of himself, works out every day and "I don't stress myself out."

> The summer of 2007 is going to be the best summer since the summer of 1996 —if you do it right.

"Don't do as I did"

Nelson Vergel was one of the treatment advocates who pushed pharmaceutical companies into a bold new era: allowing multiple experimental drugs to be taken together. This avoids sequential monotherapy, where people add only one effective drug, rather than two as recommended by specialists. Salvage patients have not had the luxury of adding two new drugs for years now.

As a result of their efforts, Merck & Co., maker of the HIV protease inhibitor Crixivan, allowed people enrolling into their study of MK-0518 (from a brand new HIV drug class, integrase inhibitor) to also take the then still experimental Prezista. And Tibotec put together two experimental HIV drugs in one study, its non-nucleoside TMC-125 and its protease inhibitor TMC-114 (Prezista), and allowed MK-0518 in its trials.

Part of Vergel's passion for salvage therapy is his own fight for survival. He has been HIV-positive for 23 years and has accumulated resistance to all HIV drugs, including Fuzeon. And so he entered the MK-0518 study, while also taking Prezista (along with the necessary Norvir booster and Truvada).

But the resistance profile for Prezista had not yet shaken out, and Vergel's expectation that his virus would be sensitive to the drug—would get knocked out by it—turned out to be wrong.

After reaching the undetectable level for the first time ever, within three weeks of entering the study, he saw his viral load rise again to 800 after 24 weeks and then 20,000 later on. It's holding steady, and is still lower than the 60,000 he started with.

His T-cells went from 182 to 420 and as of January was down to 300. "I'm still healthy," says the Houston resident, who advocates exercise and nutritional supplements for people with HIV, work that he's cutting back on to focus on salvage therapy. "I've lived for 23 years without undetectable—hell! I'm getting old!" he says with a laugh.

Vergel says the resistance profile for Prezista was not available for genotype testing until the time of its approval, and running his previous blood sample again found that sure enough, his HIV was already resistant to the drug before he went on it.

"I was really upset because integrase is so good of a class," says Vergel. "I'm the only person I know who failed in the study, even though about a third of the patients in the study had treatment failure. I think the integrase class was the best chance to get to undetectable in a long time."

Now Vergel wants others to learn from his mistake.

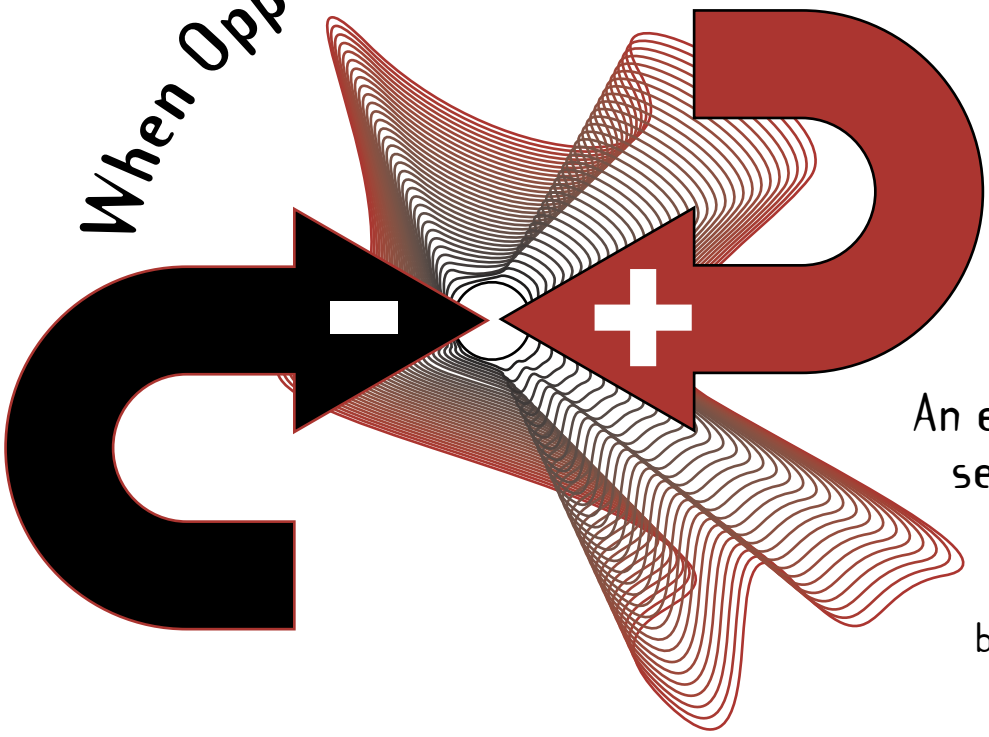
"The summer of 2007 is going to be the best summer since the summer of 1996—if you do it right," he believes. That's when MK-0518 is expected to be approved, as well as maraviroc from Pfizer, which are both now available through expanded access. (See page 25.) Maraviroc is a new type of HIV entry inhibitor drug. On their heels are other newbies: TMC-125 (also available in expanded access) and the Tanox drug TNX-355, which is from another new class, called a monoclonal antibody.

Vergel hears doctors and advocates say that this new era reminds them of 10 years ago. Vergel agrees, but says it's "dangerous" to talk about the end of salvage therapy. He says he hears people say that all the time—that people in need of salvage therapy no longer exist, that the integrase inhibitor from Merck will save them all.

"I say that HAART left a few people behind," Vergel says. "That's why I tell people, don't be left behind again. If you can wait for two or three active drugs, do so. Don't be overly aggressive if you can help it."

Visit www.salvagetherapies.org.

When Opposites Attract



An exploration of serodiscordant relationships

by Keith R. Green

Note: All names have been changed.

Alex's HIV status didn't affect Robin's decision to marry him. She loved him and, for her, that was all that mattered.

They talked extensively with doctors and numerous health educators about the risks involved with pursuing a relationship like theirs—where one person is positive and the other is negative. They understood everything that they were told, but there was nothing that anyone could say or do to curtail their love for one another. They believed they were a match made in heaven.

They learned that their kind of relationship is called serodiscordant. They also learned that it would be considerably different from the preconceived notions of "normal" relationships that they both once held—specifically as it related to the bedroom. Totally uninhibited porn star style sex would not be their reality, if Robin was to remain HIV-negative. But sex had not been what brought them together so, as Robin so proudly declares, it sure as hell wasn't going to keep them apart.

They learned that Alex should try, as often as possible, to take his medications at the exact time and at the exact dose in which they were prescribed. This would help to keep his viral load down, decreasing the risk of his transmitting the virus to Robin.

They cautiously explored the sexual playing field until they discovered fun and creative ways to keep hope alive in the bedroom. They experimented with various kinds of foreplay, sex toys, and mutual masturbation. They watched soft porn-like videos on stimulating ways to put a condom on your partner. And, because they both desperately wanted children, they researched alternative ways to pro-create, such as sperm washing and artificial insemination.

Bad luck, good luck

While the process of finding the right niche for them was more fun then either had anticipated, Alex admits that it was kind of scary at first. "I was very self conscious," he reflects. "I watched my moves very closely. I did not want to harm her in any way." As time passed, however, safer sex practices became second nature for both of them. "It got to a point where we didn't even think about it anymore," Robin says. "We just did it."

And they did it without incident, until one dreadful moment in the middle of a sporadic early morning lovemaking session when, you guessed it, the condom broke.

Words could not describe Alex's fear. "That [moment] was even harder than finding out that I was HIV-positive," he remembers. "Just the possibility that I may have infected her was way too much for me to bear."

In that instant, all of the knowledge that they had acquired since they made the choice to be together came into focus. They clearly understood the seriousness of such a mishap. But because they had been armed with knowledge of post-exposure prophylaxis, they were able to maintain Robin's HIV-negative status. (See March/April 2005 and July/August 2005.) She immediately began taking a regimen of Alex's medications until they could get her a prescription of her own. This task would prove difficult in and of itself because nobody in their country knows of Alex's HIV status.

They live in a country where it is against the law for an HIV-positive person to knowingly marry someone who is HIV-negative. Alex commutes to London every three months or so to visit with his doctor and to receive his medication. In order to avoid bringing any attention to their serodiscordant relationship, while also trying to prevent the onset of an HIV infection, Robin would have no choice but to do the same.

Today, four years later, she remains HIV-negative—as does their daughter, Lauren, who was conceived in that same

moment. The combination of routine HIV testing along with a strategic and strict plan of antiretroviral therapy given to Robin throughout the course of her pregnancy kept her and their child free of HIV. Alex and Robin credit their incredible stream of good luck to their belief in real life miracles. The scientific world credits it to the power of applied knowledge. Both may be right.

Bad luck

Unlike Robin, 22-year-old Ricardo was not so lucky (or knowledgeable). Following a night of heavy drinking and partying with a group of his college buddies, he went home with a guy he hardly knew. He knows for sure that they didn't discuss HIV status, but he genuinely does not remember whether or not they used a condom—though up until that point, he *always* insisted on using them. And though he knew the possibility of having been exposed to HIV on that solitary night, unfortunately, he knew nothing of post-exposure prophylaxis.

A couple of months later Ricardo began dating Jorge. The two had been friends for a little over a year and became incredibly close during that brief period. In fact, it was Jorge who had picked Ricardo up from the stranger's house following his drunken mishap. They hadn't acknowledged their attraction for one another because, at that time, Jorge was in a relationship (which was consistently on the rocks). Ricardo supported Jorge through the difficult break-up and it was during that period when their mutual attraction was unveiled.

Because they were friends first, they were already familiar with each other's mental and emotional make-up. So they spent their first couple of weeks as a couple exploring each other's physical likes and dislikes. They decided to go together to be tested for HIV and other STIs (Sexually Transmitted Infections), before taking the relationship to the next level. Jorge admittedly hates using condoms and, before either of them could agree to a committed condom-less relationship, they wanted to be sure that it was safe to do so.

Neither expected his test to come back positive (despite Ricardo's previous mishap and Jorge's disdain for condom use), but Ricardo's did. And while Jorge fully understood that they would have to approach their sex life in a totally different fashion than originally planned, he assured Ricardo that his HIV status would not alter his decision to be with him.

Dr. Bell's Safer Sex Spectrum

Dr. Margo Bell in Chicago (see November/December 2005 cover story) spends a great deal of time in her practice educating people about safe and *safer* sex. In theory, she believes, safe sex can only occur if you have never had any type of sexual contact with another person before *and* you know for sure that your first partner has not either. Safe sex includes masturbation, mutual masturbation, grinding with clothes on, showering together, and other activies that do not involve the exchange of body fluids.

Safer sex, on the other hand, involves decreasing your risk of transmitting any type of Sexually Transmitted Infections (STIs) or preventing pregnancy by using some type of method or barrier. For her patients, she constructed the scale below which rates the level of risk involved with certain sexual behaviors. Although it is not all encompassing of the multitude of sexual behaviors that exist in the world, it is general enough for anyone to find themselves and what they like within it.

Male/female sexual risks (from most risk to least)

- anal sex without a condom (most risk)
- vaginal sex without a condom
- oral sex without a condom/dental dam
- anal sex with a condom
- vaginal sex with a condom
- oral sex with a condom/dental dam
- mutual masturbation or intimacy without exchanging body fluids (least risk)

Male/male sexual risks (from most risk to least)

- receptive anal sex without a condom (most risk)
- insertive anal sex without a condom
- oral sex without a condom/dental dam
- penis to penis sex (where urethras touch together)
- anal receptive with a condom
- anal insertive with a condom
- oral sex with a condom
- mutual masturbation or intimacy without exchanging body fluids (least risk)

Female/female risk

Although there is very minimal risk of HIV transmission associated with female-to-female sexual contact, Dr. Bell does encourage the use of sterile dental dams for oral sex as well as the sterilization of all sex toys prior to each use. She also recommends new toys be utilized at the onset of play with new sexual partners.

Dr. Bell says that she always stresses to people the importance of knowing the HIV status of their sexual partners and for the HIV-positive partner (if there happens to be one) to be on, and adhere to, HIV medications. She also encourages them to understand how post-exposure prophylaxis works and how they can go about accessing it in the event of an emergency. (See March/April 2005 and July/August 2005.)

She encourages gay and bisexual men to consider having conversations about "positioning"—where what happens in the bedroom between a serodiscordant couple is determined by HIV status. So, for example, the HIV-negative partner would be positioned primarily in the insertive role of anal sex (with a condom), because there is less risk involved than being in the receptive position, in the event that the condom should happen to break.

Her motto: Informed dialogue leads to informed decisions. "Know the facts and have fun," she says with a smile.

"We'll get through this," he said, comforting Ricardo. He loved Ricardo and, for him, that was all that mattered.

At first, things were relatively easy for the two of them as it concerned sex—they simply weren't having it. Ricardo, emotionally distraught from recently learning of his HIV status, was not feeling up to it and was even more terrified at the thought of infecting Jorge. Jorge understood, remaining supportive and patient as Ricardo processed this life-altering situation. He admits, however, that he did not share Ricardo's fears. "My concern was for him and how he was doing," he says. "For the most part, he had been the safe one. I was the one who did not like to use condoms. It was all really overwhelming. My main concern, though, was to make sure that he was okay."

As time moved on, the initial trauma of learning that one of them was HIV-positive began to subside. The "newlyweds" found themselves anxious to bring their sexy back. "We didn't know what we could do," Ricardo recalls. "I didn't want to do anything at all to put him at risk, so every little thing became a big deal." He even insisted that they not shower together anymore because he was afraid of passing the virus on to Jorge.

Looking back now, they realize just how absurd some of their fears were. The reality, however, is that they are not alone. Of the many interviews conducted on the subject for this article, Alex and Robin were by far the exception. Many people, both HIV-positive and negative, lack proper knowledge of safer sex practices (outside of abstinence and consistent condom use) and post-exposure prophylaxis. Most don't understand the real risks involved with a "typical" sexual experience. Others understand those risks all too well and, as a result, have altogether lost their zeal for having a sex life.

Other views

"I just don't have sex anymore," an HIV-negative interviewee (whom we will call Mike) said frankly. "It's just not worth it."

This 30-something year old gay man finds his release through his on-going quest to find the world's most exotic porn. "It's become a hobby, really, bordering on addiction. I collect all different kinds of porn—from amateur straight to extreme gay bestiality type stuff. I really enjoy it all." He's been celibate for over three years and says that he honestly has no desire for sex with another person right now.

On the other end of the spectrum, however, others have thrown caution to the wind and are having what they say is the best sex of their lives.

"I have more sex now than I ever have," said Roxanne—a 32-year-old, bisexual, HIV-positive woman from Chicago's South side. "I have sex with men and women who are, for the most part, HIV-negative. I keep myself and my partners educated. I try to keep my viral load at an undetectable level and I always disclose."

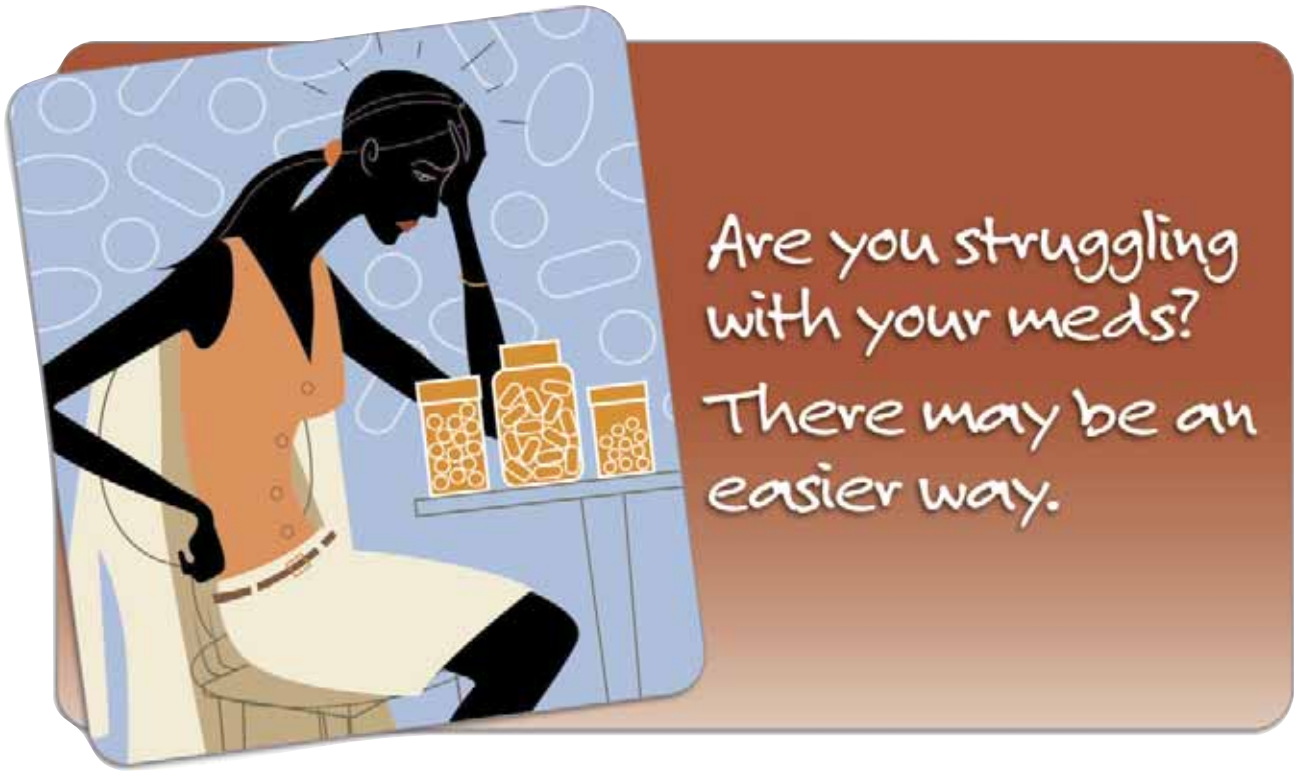
Roxanne, who is not necessarily interested in a monogamous relationship and currently has multiple male and female sex partners, says that she finds that her HIV status is often not an issue for people—particularly HIV-negative straight men.

"I've only been rejected one time, and that was because I didn't take the time to educate the gentleman about the risks involved," she says, almost too confident. "Had I done that, there would have been no way he could have rejected me."

To her knowledge, Roxanne has never infected another person with HIV. "And the people I deal with, especially the men, *hate* to use condoms," she says. While the risk of contracting other STIs or becoming infected with a different strain of HIV is always in the back of her mind, she feels that her "sexual revolution" is what helps to keep her spirits up as she copes with living with a chronic disease.

"Living with HIV is no shopping spree on the Magnificent Mile," she says with attitude. "But it doesn't have to be a nightmare on Elm Street either. I do what I do, how I like to do it. I understand the risks involved and, if I ever feel the need to change, I will. Right now, this is what works for me."

Don't lose yourself to your meds HIV.



Too many pills, too many times a day is a problem for many people with HIV. The fewer pills you have to take each day, the easier it may be to manage your HIV.

Do you ever forget to take your meds? It happens to the best of us.

Missed doses can be a sign that your regimen isn't convenient for you. If you're missing doses, think about these questions and answers:

Q: Is there a simpler regimen I can take?

A: There are several once-a-day meds available—talk to your healthcare provider.

Q: Are there once-a-day meds that don't have food restrictions?

A: Some once-a-day meds allow you to take them with or without food.

Q: Can I change meds and stay undetectable?

A: There are studies showing that people can change one or more of their HIV meds and stay undetectable.[1-3]

Keep your virus under control and simplify your regimen.

If your viral load is undetectable and your CD4/T cell count is up, then why are you letting your pills get in the way? It may be time to talk with your healthcare provider about **once-a-day meds**.

Don't let your meds run your life. For more information, visit **www.MyHIVLife.com**.

Learn more at

MyHIVLife.com

References: 1. Moyle GJ, Sabin CA, Cartledge J, et al. *AIDS*. 2006;20:2043-2050. **2.** Carr A, Workman C, Smith DE, et al. *JAMA*. 2002;288:207-215. **3.** Drechsler H, Powderly WG. *Clin Infect Dis*. 2002;35:1219-1230.

Part of an ongoing series from Gilead

Resisting Resistance

A long road of unintentional missteps pays off

by Matt Sharp

When I was diagnosed with AIDS in 1991, I never dreamed I'd reach forty. This past summer I reached the age of fifty. It seems I have lived a long battle with HIV. Little has been easy about survival. It has taken a concentrated and impassioned effort to gain every piece of knowledge I could in order to stay ahead of a deadly virus, one that has a basic survival instinct not unlike my own. I am the consummate salvage AIDS patient with an ironclad will to survive.

AIDS drugs have changed the course of the epidemic in a relatively short time, and have played a huge role in my survival, as with thousands of others. My treatment history reflects AIDS research progress and pitfalls. Over the past 18 years my virus first became resistant, then highly resistant, and now what we call multi-drug resistant (MDR). Doctors use the same terminology in tuberculosis usually signifying a more serious condition, one that is difficult if not impossible to treat. In HIV the condition is problematic not only because it becomes difficult to treat, but because MDR HIV can be transmitted to other people. Fortunately, however, I have lived quite a long time with MDR HIV, and have found new treatment options that I never thought possible.

Several new drug classes are showing promise and have reached final stages of development.

What I didn't realize when I began HIV treatment was that I was putting together a recipe for disaster. The way we use antiviral drugs today had to be learned over time, and even though I was fortunate enough to gain access to the new discoveries, I was using them incorrectly. Each time I added a new drug to another older medication I was creating a more mutated virus.

For someone with MDR, finding a new treatment today is complex but not impossible. If anything, there is new hope now to treat those of us who are multi-drug experienced. My treatment history has been a roller coaster of decision making and considerable frustration trying to find effective drug combinations. In some ways it's been like a long war waged against many improbable foes. I have had to consult with many doctors, haggle with drug companies, sustain risk through several clinical trials, and even get arrested in civil disobedience to gain access to drugs that have kept me alive.

But recently, my options have gotten better due to a resurgence in HIV drug development. Several new drug classes are showing promise and have reached final stages of development.

For years I have stayed alive on what is known as monotherapy, since I had to add one new drug onto the backbone of drugs I was already resistant to. It's been the bane of my existence since the early days of my HIV treatment, trying to find two active drugs to work against my crafty and persistent virus. We know now that at least two active drugs are needed for people to have the greatest control over HIV replication.

Looking back, in 1989 I began treatment with AZT, now known as Retrovir. It was the only HIV drug available then but doctors did not know the right dose of it to prescribe. AZT is somewhat famous, being the cause célébré of an AIDS activist movement on Wall Street and at the FDA. I was one of many who started using it as monotherapy, thus starting my resistance cycle and mistaken treatment course of *sequential* monotherapy. But back then, it was all we had.

After using AZT for several months I gained access to ddC (Hivid, now discontinued) from an AIDS Buyers Club and began my first dual regimen, not understanding that I was only getting a small effect from ddC, if at all. I probably had developed resistance to AZT. This enabled my HIV to replicate, creating mutations to occur and a ride on my resistance roller coaster.

During the next few years of my treatment history, I tried a lot of complementary therapies, adding drugs as they became available. I took drugs like Videx and Zerit, adding each of them to whatever I was taking. So essentially I was building new mutations and using only one effective drug at a time. This went on for several years as I slowly watched my T-cells drop.

I gained access to Rescriptor, the first of a new HIV drug class called non-nucleoside reverse transcriptase inhibitors. That unfortunately was another one of my big mistakes. Newer drugs in the NNRTI class are more potent and easier to take than Rescriptor, but I needed this drug as it came first. So, I eventually became resistant. What we didn't know at the time is that the drugs in the NNRTI class would be highly cross resistant to each other. If you develop resistance to one you blow the whole class.

I became very angry and frustrated at that time. I joined ACT UP and chained myself to drug company doors to demand better HIV drugs. As far as I was concerned, the government and research institutions could never move fast enough when everyone I knew was dying.

By 1994, HIV was having an effect on me. I was wasting, lost over 20 pounds, and began developing other symptoms. I was afraid. Wasting zaps your energy and does not give you much self confidence in surviving. Skull-like faces and "AZT butt"—severe loss of the buttock muscles, were noticeable everywhere in the Castro district of San Francisco.

Then human growth hormone saved my life in a double blind placebo controlled study, despite the fact that I received the placebo for the first part of the trial. I regained my weight and enrolled in the first protease inhibitor study of saquinavir (Invirase). The background drugs in this study were AZT and ddC—two drugs I had already used. So with saquinavir the only active drug, I was once again getting the effect of monotherapy. It was a big disappointment for me and I remained in search of something new.

Next I signed up for the Crixivan study and for the first time saw my virus levels drop. But again I had to use background drugs that I had used before, receiving Crixivan monotherapy. In no time Crixivan failed and my T-cells slumped.

I learned about research and the clinical trials process through my actual experience and with a sub-committee of ACT UP Golden Gate. A group of us held an immune-based therapies breakfast club on Saturday mornings where we would pore over the latest journal articles and hear from graduate students and researchers from Stanford and UCSF. It led me to consider my treatment course a little differently. Up to this point every drug had failed and I realized what I needed was something to boost my weakened immune system.

I joined a very progressive thymus transplantation study in hopes of restoring some thymus function, which plays an important role in the immune system. I was flown across the country and underwent an overnight hospital stay where thymus tissue was transplanted into my abdomen.

The thymus tissue was not rejected by my weakened immune system, still, despite the transplant, my T-cells continued their slow decline. I tried other new protease inhibitors as they became available and began "recycling" my medications, reusing past drugs I was most certainly resistant to. I was technically on HAART (Highly Active Antiretroviral Therapy), but it would probably best be described as only *partially active* for me. Whatever the strategy became, I luckily remained fairly healthy until late 1999.

As an AIDS treatment activist I had been invited to a community meeting with Trimeris, the company that discovered Fuzeon, then called T-20. It was one of the first community meetings of this new drug class targeting the point where HIV "fuses" into the T-cell. I was fascinated by the new concept and hopeful that someday the drug may work for me. It offered me and people like me who had developed MDR virus possibilities for a new option from a whole new HIV drug class. I followed T-20 development closely.

In 2002 I enrolled in the pivotal T-20 clinical trial at Northwestern, only after haggling investigators and Roche to get the study started. My bad luck landed me into the arm that did not receive T-20. But fortunately, the study design enabled me to roll over to receive T-20 after 24 weeks. After I started the drug my viral load went undetectable for the first time ever…but for just one week. I was resistant to the background regimen, so the T-20 was working alone, only to quickly develop resistance. Strangely enough I was as healthy as I could be and even started back to work.

My numbers started changing for the worse after three years on T-20; I was most likely resistant. I learned about studies of a couple of new protease inhibitors that companies claimed were not cross-resistant to the older protease inhibitors. One of those drugs was tipranavir—now called Aptivus.

T-20 and tipranavir plus my background regimen of Truvada enabled me to stay relatively healthy and with the lowest detectable viral load ever, but my T-cells unfortunately dropped below 100. For me all good things in HIV come to an end, but new drugs were on the horizon.

Studies began on two completely new drug classes, integrase inhibitors and co-receptor antagonists. These studies would afford me the option of adding TMC-114 (brand name Prezista), the one protease inhibitor I had not tried. I entered the Merck MK-0518 study and for the first time since I started HIV drugs I would have two new drugs! After two months I have undetectable virus levels and the highest CD4 count since I first started therapy, at more than 200. Finally, I have treatment success after the long haul of disappointments and frustration.

People with MDR virus should hold on as long as they can until they can gain some of the new agents being studied—at least two new drugs.

Certainly people starting HIV treatment today will not need to go through the difficult road I did, ending up with a MDR virus and few options. The prospects are much better for choosing a regimen out of the 26 drugs that will be strong, safe, and long lasting. People with MDR virus should hold on as long as they can until they can gain some of the new agents being studied—at least two new drugs. The possibilities will open up if people can just wait. Unfortunately, there are those who can't.

It takes a lot of knowledge and luck to fight this tricky little virus called HIV. People must be persistent and demand what they need. They have to work closely with an experienced HIV doctor and be aware of all their options. They have to read up and study. Ask questions. Dare providers to do the right thing for you. It can be done. I truly believe I am alive today not because of the mistakes I made in treatment choices, but because I was resilient and informed enough to buy time to this very day.

Survival can be a desperate thing. If you became stranded on a desert island, you would do whatever you had to stay alive. I think it is no different in living with HIV. But today, due to research breakthroughs, new drug development and a little determination, patience, and awareness, a longer life with HIV is attainable… it is a chronic manageable disease.

Adapted from an article which appeared in the Spring 2006 ACRIA Update.

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For People Living With HIV

Announcing the

TMC125

U.S. Expanded Access Program

Tibotec Pharmaceuticals Ltd., introduces an expanded access program for TMC125, its investigational NNRTI for the treatment of HIV infection.

An expanded access program provides investigational drug therapy to eligible patients while the drug is still under review by the FDA

This program is open to HIV-1 infected adults who

- **Are at least 18 years of age**
- **Have received treatment from at least 3 classes of licensed oral ARVs (N[t]RTIs, PIs, NNRTIs), including 2 different PI-based regimens**
  - **— Primary NNRTI resistance with 2 class ARV experience (N[t]RTIs, PIs) permitted**
- **Have limited treatment options due to virological failure or intolerance to multiple ARV regimens**
- **Are unable to use currently approved NNRTIs due to resistance and/or intolerance**
- **Have not participated previously or currently in the Tibotec-sponsored DUET trials**

Patients can participate if they meet the eligibility criteria specified in the study protocol.

The safety and efficacy of TMC125 has not been established.

TMC125 does not cure HIV infection/AIDS or prevent transmitting HIV to others

For more information, ask your healthcare professionals to:

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E-mail **TMC125EAP@i3research.com**
Visit **www.tibotec-eap-usa.com**

tibotec

WHAT THE WORLD NEEDS NOW

NEW HIV DRUGS FOR THE NEXT DECADE

BY BOB HUFF

The greatest unmet medical need in HIV medicine worldwide is for better treatments for people starting treatment for the first time (treatment-naïve patients). The world has made great progress in bringing antiretroviral (ARV) drugs to more than a million people in Africa and elsewhere in the developing world during the past few years. Yet, with 40 million people infected worldwide and perhaps a quarter of them in immediate need of therapy, huge gaps remain in the availability of treatment, and over 7,000 people with HIV continue to die everyday.

The most widely used ARV regimen in the developing world contains nevirapine, stavudine, and lamivudine (in the U.S., brand names Viramune, Zerit, and Epivir). Although this combination is highly effective in suppressing HIV, its low cost and availability in easy-to-use combination pills from a number of generic manufacturers are the key factors determining its widespread use. If it were not so affordable, this drug regimen would likely not be one's first choice. In 2004, stavudine was removed from the list of preferred first-line drugs in the U.S., and nevirapine has never appeared on that list. The standard first-line HIV regimen in the developing world urgently needs a second look.

HIV DRUG DEVELOPERS STILL HAVE IMPORTANT WORK AHEAD OF THEM.

Stavudine (d4T), although highly effective as an anti-HIV drug, has been associated with body fat changes known as lipoatrophy, and may have been one of the chief culprits in the epidemic of facial fat wasting that affected so many people on ARVs during the first decade of HAART. After only a few years of widespread use in the developing world, reports are starting to appear of body fat abnormalities in patients in Lesotho, Thailand, and elsewhere. The appearance of such highly visible side effects in people taking ARVs has the potential to damage a sometimes fragile public perception of HIV treatment. It would be tragic if ARVs came to be shunned in some communities because they were seen as the source of disfiguring and stigmatizing side effects. Another serious side effect of stavudine use in some patients is painful peripheral neuropathy, which can cause painful and burning sensations in the toes and fingers. Zidovudine (AZT), a more expensive cousin of stavudine, is an alternate drug choice, although it too has been associated with the development of fat wasting problems, albeit at a slower pace. Zidovudine also can contribute to anemia, a serious problem for pregnant women and many others in the developing world with suboptimal nutrition.

Tenofovir (Viread in the U.S.) is now the most commonly used replacement for stavudine and zidovudine in the rich countries because it is highly effective and causes no serious side effects in the great majority of people using it. Although tenofovir does not have tolerability problems, it has been associated with a reduction in kidney function and possibly with diminished bone mass, side effects that are mild and stable in most people but give doctors a bit of worry and require monitoring, especially in patients with prior kidney problems. Unfortunately, careful monitoring is a luxury that can not be depended upon in resource-poor settings, although clinical trials of tenofovir in Africa have not uncovered any serious problems when using the drug in routine practice under limited conditions. One formidable problem, how-

ever, is that tenofovir is many times more expensive than stavudine, and although future competition between generic manufacturers may lower the cost, tenofovir will likely never be as cheap as the current standard. For the foreseeable future, the developing world is stuck with stavudine.

THE STANDARD FIRST-LINE REGIMEN IN THE DEVELOPING WORLD URGENTLY NEEDS A SECOND LOOK.

The non-nukes

In the North, initial non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens are most commonly anchored with efavirenz (Sustiva in the U.S.) and backed up by tenofovir and emtricitabine (a drug very similar to lamivudine). These three drugs are also now available in a convenient, once-daily, single tablet from their brand name makers.

As anchor drugs of an NNRTI-based regimen, both nevirapine and efavirenz share many similarities. They both effectively control HIV and both remain in the bloodstream for extended periods. But both are also susceptible to loss of activity if HIV develops only one or two resistance mutations, and developing resistance to one drug results in resistance to the other. In the rich countries, efavirenz is more commonly prescribed because it is considered more potent and because nevirapine requires much closer monitoring when initiating the drug in first-time patients due to severe and occasionally fatal liver problems that have developed in a few people. Nevirapine should not be initiated in women with CD4 counts higher than 250 cells/mm3 or in men with CD4 counts higher than 400 cells/mm3. Nevirapine is also a difficult drug to use in combination with certain drugs used to treat tuberculosis, one of the most deadly coinfections in the developing world.

But even the best available choices for privileged patients in the North leave much to be desired. Efavirenz is a convenient and highly effective drug and most patients probably find it trouble-free over the long-term. But efavirenz causes profound sleep disturbances and exhaustingly vivid dreams for many people who may tolerate these side effects for a year or so, but are relieved when finally switched to something else. And because efavirenz has been associated with birth defects, it should not be used in women who are or want to become pregnant. For them, nevirapine or a protease inhibitor is a safer choice.

In the developing world, the best price for an efavirenz-based combo is five-times that of a generic nevirapine regimen which, for a national treatment program, means that fewer people can be treated and the population-wide impact diminished. Basing a regimen on a protease inhibitor adds additional costs. For mass treatment programs conducted with limited public health resources in very poor countries, pennies per day matter, and the best price for the best available regimen is often out of reach.

After the first drugs are gone

Because resistance to nevirapine is relatively easy to produce, and because nevirapine resistance also eliminates efavirenz as an option, there is already a growing need for second-line therapies based on the protease inhibitors for treatment programs in the developing world. This need has not received a lot of attention, partly because of the urgency of getting first-line therapies rolled out to those who desperately need them, and partly because the tools for monitoring first-line treatment failure are not widely available outside of a few well-resourced ARV treatment programs like the U.S. government's PEPFAR. But when the need for switching patients to protease inhibitors is confronted it immediately becomes apparent that the cost of treatment rises dramatically. The cheapest, most practical, and most widely available protease inhibitor in the developing world, Abbott's Kaletra, is four to five times more expensive than nevirapine, even when obtained through the company's no-profit pricing program for the developing world.

While there is an unmet medical need for safer, cheaper, more potent, more durable, and more tolerable HIV drugs for all of the world's HIV patients, it is the crushing burden of HIV in the developing world that now underscores the urgency of finding better ARV drugs.

Characteristics of an ideal regimen

Obviously an ideal new drug for treating HIV in the developing world must potently suppress HIV replication. But it should also work against a broad range of HIV subtypes and against virus that has lost susceptibility to other drugs. Ideally, a new drug would target a unique point in the viral lifecycle so critical to HIV's survival that resistance mutations would be rare, or, if they occurred, would produce a drastically impaired virus. An ideal drug should remain in the bloodstream long enough to allow once-daily dosing—and be relatively forgiving of the occasional missed dose. Optimally, the drug would be so potent that it could be used on its own, without NRTI support. Alternatively, it would be easy to formulate together with other HIV drugs into a single pill without any special technology.

It should also enter and pass through the body without affecting the blood levels of other drugs or being much affected by them in turn. Not only should the long term safety profile of this ideal drug be benign, but it should have few of the tolerability discomforts like mild nausea or diarrhea that accompany so many other drugs. Doc-

EVEN THE BEST AVAILABLE CHOICES FOR PRIVILEGED PATIENTS IN THE NORTH LEAVE MUCH TO BE DESIRED.

tors need to feel confident that they can start a patient on this drug and not have to follow up for several months or more. The need for monitoring should be minimal. Patients need to know that the drug can reliably roll back their HIV disease without making life miserable or increasing their risk for experiencing other medical problems.

Finally, an ideal new ARV for the developing world must be cheap and easy to manufacture, and the patent holder must be willing to allow multiple generic manufacturers to make abundant quantities available wherever they are needed. A wonderful drug like this would be in demand in the rich countries too, and that's where the innovating company would expect to make its investment pay off.

Coming in 2007

This set of specifications is a tall order, but there are encouraging signs that better drugs are in the pipeline. Merck is racing forward with development of a new drug that works by inhibiting a unique target in the HIV lifecycle called integrase. So far, Merck's integrase inhibitor appears to be quite potent and has not revealed any particular safety problems (day-to-day tolerability remains to be seen, with some trial participants complaining of increased flatulence). A minor drawback for Merck's first offering in this new drug class is a requirement for twice-daily dosing. The biggest medical unknown yet to be answered by the clinical trials in progress is whether or when resistance mutations will arise that defeat the drug. The biggest commercial unknown is how much it will cost to manufacture the integrase inhibitor, how much Merck will charge in the developing world, and what will be the company's policy on allowing third party generic drug makers to produce the drug for low-profit markets. Merck's integrase inhibitor may receive U.S. approval by late 2007.

Another new drug due in 2007 that also blocks HIV infection in a unique way is Pfizer's entry inhibitor, maraviroc, a CCR5 antagonist that prevents the virus from entering target CD4 immune cells. Although data is still sparse, in preliminary studies, the drug was effective, and no safety or tolerability issues have emerged so far. One limitation is that maraviroc is only effective at blocking HIV that uses the CCR5 coreceptor to infect new cells. HIV variants that use a different coreceptor are not inhibited by the drug, and these variants may be present in 10% to 60% of people with HIV, mainly depending on how long they have been infected. This means that maraviroc may not be reliable for use in broad populations without specialized and expensive diagnostic tests.

New NNRTIs are also being developed by Tibotec that address problems with nevirapine and efavirenz, and TMC-125 (etravirine), also due in 2007, may be useful in communities where primary, transmitted nevirapine resistance is a problem.

There is an unmet medical need for better HIV drugs for initial and subsequent therapy for all kinds of patients, in all parts of the world. A drug with ideal qualities for the developing world would also be what is needed in the North by treatment-naïve patients and by highly treatment-experienced patients who have developed resistance to nearly all of the 20-plus HIV drugs available to them. New drugs on the visible horizon may meet some of these criteria but the ideal is still out of reach. Barring the surprise discovery of an effective vaccine or some other unexpected breakthrough, HIV drug researchers still have a lot of important work ahead of them.

Early Access to Coming Drugs

Expanded access programs have opened to offer early access to three experimental drugs expected to be approved during 2007.

Contact your doctor or call for more information

TMC 125, an NNRTI from Tibotec Pharmaceuticals
866-889-2074; www.tibotec-eap-usa.com

MK0518, an integrase inhibitor from Merck
877-EARMRK1; www.earmrk.com

Maraviroc, a CCR5 antagonist from Pfizer
888-275-4478; www.maraviroceap.com

Bob Huff is the Editorial Director of Treatment Action Group in New York City. Reprinted with permission from the December 2006 Issue of TAGline.

A version of this article first appeared in GMHC Treatment Issues.

Managing Longterm Side of Effects of HIV Therapy

What to look for and tips to use

by Maurice W. Oelklaus, DO, FAAFP, Charlott L. Williams, RN, CCRC, and Patrick G. Clay, PharmD

You've come a long way, baby

Antiretroviral therapy (HAART, ART, or anti-HIV medicines) has indeed come a long way in the last 25 years. ART has allowed for individuals who are HIV-positive to live longer lives. New ART medicines and classes of ART have been created to help in the fight against HIV. The development of new classes of ART allows for the virus to be attacked in different ways. Not attacking the virus from different directions at one time has shown us time and again to not work. So combining ART has worked, but at a price.

No such thing as a free lunch

ART, just like medicines for high blood pressure, cholesterol or even acne can cause side effects. Some of these occur after you take your first dose. As a matter of fact, it is common to experience some side effects when starting ART. The good news—most of these side effects get better or go away in about a month or so. Your body just has to adjust. Still, it is very important to take antiretroviral medication every day. You need to learn what to do to make these as tolerable as possible. Other side effects may not show up until you have been on the medicine for a long time. In some cases, the side effects may be related to the class or group of ART they are in. This article focuses mainly on those side effects that take a while to show up.

The nukes

Nucleoside reverse transcriptase inhibitors (nucleoside analogs, NRTIs, or nukes) were the first class of antiretroviral medications created. Drugs in this category are: Combivir, Emtriva, Epivir, Epzicom, Retrovir, Trizivir, Truvada, Videx, Viread, Zerit, and Ziagen. Nukes can cause swelling of the pancreas or liver, changes in your body's acid and base balance (lactic acidosis), alteration of fat deposits and even anemia. We can't cover all of these here, so be sure to talk with your doctor, nurse or pharmacist.

Pancreatitis: Since your pancreas helps to digest your food, it needs to send out certain chemicals after you eat. Some drugs can cause your pancreas to swell, not allowing these enzymes to come out at the rate they should. Who is at greater risk is not really known. There is some information that if you have had pancreatitis in the past, you are more likely to get it again. Those patients who drink alcohol—especially binge or party drinking—are at higher risk. If you have diabetes or some other medical conditions, you could also be at risk. Some patients report using vitamin E and C, calcium, vitamin B12, and folate to prevent it. Some nukes are known to cause this more than others, so ask your doctor, nurse or pharmacist questions when you pick up your meds.

Hepatitis: The liver can also become inflamed when taking nukes (or the other classes too—see below). Nukes may cause extra fat to be deposited in the liver. To be sure, the best way to prevent this from happening or getting worse is to not drink alcohol. Why? Alcohol is broken down in the body by the liver, so the harder the liver has to work, the more inflamed it can become. Just like other medicines, nukes need liver enzymes to work. The more things in the body the liver has to break down (like alcohol) the harder the liver has to work. Believe us, you want the liver to have the energy to break down your medicines and not waste energy on other things. A build-up of nukes in the body is a bad thing. It's not just alcohol. Even those non-prescription or herbal medicines count! Just like we said before, your doctor, nurse or pharmacist can help you understand this better.

Lactic acidosis: Yes, this is what killed Private Santiago in "A Few Good Men," but you can definitely handle the truth. Seriously, this is a bad deal if it happens. Lactic acidosis occurs when the lactic acid in your bloodstream becomes too high. Thankfully, this is a rare side effect but the only way to make sure it is not happening is to make sure you have good, consistent follow-up with your healthcare provider. Lactic acidosis can sneak up on you. Some patients report coenzyme Q10, riboflavin, thiamine, and L-carnitine prevent lactic acidosis from occurring. Be on the safe side and ask your healthcare provider when you are there for your follow-up.

Lipoatrophy: To be perfectly honest, we can see this with just about any ART class. Many experts feel Zerit and Retrovir (AZT) are the biggest culprits, but there is information on almost every drug causing it. More information on this side effect is in the protease inhibitor section.

The non-nukes

Another important ART class is the non-nucleoside reverse transcriptase inhibitors (non-nucleoside analogs, NNRTIs, or non-nukes). The non-nukes are Sustiva, Viramune and Rescriptor. Sustiva has proven to work as well as any other drug out there, so it is the one most often used. These drugs can cause many of the same problems as the nukes, but for hepatitis there is specific information available for Viramune.

Hepatitis: Viramune's affect on the liver is probably the best described. You can see this more often in women—especially in those with high T-cell counts and after you have taken it for while. Just like the lactic acidosis, you can't really "feel" this coming on. If it does develop, you need to call your doctor right away. Basically what we see with Viramune is your

liver enzyme levels begin to go up. This happens most often over the first four months or so. If your doctor sees this, they stop this medicine and change it. If you don't follow-up and this continues, you put your liver at risk. Some signs of this are:

- general ill feeling or "flu-like" symptoms
- dark urine (tea colored)
- pale stools (bowel movements)
- tiredness
- nausea (feeling sick to your stomach)
- pain, ache, or sensitivity to touch on your right side below your ribs
- lack of appetite
- yellowing of your skin or whites of your eyes

If you are on Viramune and you think these are happening, call you doctor right away!

The protease inhibitors: "With great power, comes great responsibility"

This ART class (protease inhibitors, PI) is why so many people are *living* with HIV instead of dying from AIDS. Drugs in this class are Aptivus, Crixivan, Invirase, Kaletra, Lexiva, Norvir, Prezista, Reyataz, and Viracept. However, PIs have also created some of the most undesirable side effects. What do we worry about with the PIs? Increases in cholesterol and triglycerides, lipoatrophy / lipodystrophy, developing or worsening of diabetes, high blood pressure, heart attacks, bone changes and even stroke have now all been reported with the PIs. We can't cover them all, so be sure to talk with your healthcare provider.

Cholesterol / triglycerides: Increases in cholesterol and triglycerides increase your risk for high blood pressure, heart disease, and stroke. The best way to treat these is to prevent it or lower your risk as much as possible. Best way to do this? Eat a diet low in fat and avoid large amounts of starches at one time. Throw away the remote and walk to the TV. Exercise daily, take fish oil and *stop smoking*! If these can't prevent it there are prescription medications available.

Lipodystrophy / lipoatrophy: This is redistribution (or shifting) of fat in the legs, arms, buttocks (women mostly) and face; and/or gaining fat in the neck and abdomen. It's not real clear how to best prevent it, but eating a low-fat diet and regular exercise show the most promise. When it happens, some doctors stop the PI and switch to another ART class. Sculptra, a facial filler, is a new option, but you will need to find a plastic surgeon in your area who does this, and it is only a temporary fix.

Diabetes: This is a rise in your blood sugar. If this happens for a long enough time, it leads to diabetes. The best way to prevent this is by eating a diet low in sugars and carbohydrates. Another good way—exercise! If diet and exercise are not enough, prescription medications can also be an option.

Bone changes: PIs may cause a loss of bone density (osteoporosis) or bone breaking down (osteonecrosis). More information is being learned daily about this and how to best prevent and treat it, but you need to ask your healthcare provider how they are watching for this. For your part, performing weight-bearing exercises, maintaining a healthy weight, and not smoking will help decrease the loss of bone density.

Fusion inhibitors

Fuzeon is the only fusion inhibitor out there. It was the latest ART class approved and has to be injected under your skin (like insulin) twice a day. Rashes, knots under the skin, red/inflamed skin, pain at the injection site, and a bad taste in your mouth all are side effects that we see with Fuzeon. Pneumonia may occur more frequently if you are on Fuzeon so ask your doctor for a pneumonia shot (this is in addition to a flu shot). Here are some tips that may help to reduce side effects:

- Shower just before injecting. This softens the skin and may decrease the chances of reaction.
- Wash your hands! Make sure your hands are disinfected. Just before pinching the skin, use a hand sanitizer.
- Just a pinch will do! Place a small area of skin between your index finger and thumb and inject in that area. This prevents muscle injection and decreases a reaction to the area.
- Massage anyone? Massage the injection site. Do this for at least five minutes after a shot. It may help the medicine absorb into the tissues.
- Rotate! Be very careful to use a different injection site for each injection.
- Hang loose! Wear loose fitting clothing that doesn't rub against the area you just injected or an area that may be red and swollen.
- Bad taste in your mouth? Rinse your mouth with salt water, suck on sugar-free gum or mints, use plastic utensils if you have a bitter metallic taste when eating.
- Not hungry? Even if you don't feel like eating, try to have frequent small meals throughout the day. If constipation occurs, add fiber to your diet by increasing the amount of vegetables, fruits, and whole grain breads. Prune juice and apple juice will also help reduce constipation.

The best way to effectively cope with the side effects of anti-HIV drugs is to know what to expect. Be active in your doctor's visits and make sure they answer all of your questions. Knowing how to best handle side effects not only makes it easier to take the medication correctly, but feeling better will enable you to have more enjoyment from life.

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Indication[1]

KALETRA® (lopinavir/ritonavir) is always used in combination with other anti-HIV medicines to treat people with human immunodeficiency virus (HIV) infection. KALETRA is a combination of two medicines. They are lopinavir and ritonavir. KALETRA is a type of medicine called an HIV protease (PRO-tee-ase) inhibitor. KALETRA is for adults and for children age 6 months and older.

Once daily dosing of KALETRA in combination with other anti-HIV medicines is not recommended for people with previous HIV treatment and has not been evaluated in children (6 months to 12 years of age).

Important Safety Information[1]

KALETRA does not cure HIV infection or AIDS and does not reduce the risk of passing HIV to others.

KALETRA should not be taken by patients who have had an allergic reaction to KALETRA or any of its ingredients, including lopinavir or ritonavir.

Taking KALETRA with certain drugs can cause serious problems or death. KALETRA should not be taken with dihydroergotamine, ergonovine, ergotamine, and methylergonovines such as Cafergot,® Migranal,® D.H.E. 45,® Ergotrate Maleate, and Methergine, as well as Halcion,® Hismanal,® Orap,® Propulsid,® Seldane,® or Versed.®

KALETRA should also not be taken with rifampin, also known as Rimactane,® Rifadin,® Rifater,® or Rifamate®; or with Flonase,® Mevacor,® Zocor,® or products containing St. John's wort *(Hypericum perforatum)*. Once daily KALETRA should not be taken with Agenerase,® Sustiva,® Viracept,® Viramune,® Dilantin,® Phenobarbital, or Tegretol.®

Particular caution should be used when taking Viagra,® Cialis,® or Levitra,® since the interaction with KALETRA may result in an increase in their related side effects. Discuss all medicines, including those without a prescription and herbal products you are taking or plan to take, with your doctor or pharmacist.

Pancreatitis and liver problems, which can be fatal, have been reported in patients receiving KALETRA. Tell your doctor if you have nausea, vomiting, or abdominal pain, which may be signs of pancreatitis, or if you have or have had liver disease such as hepatitis B or C.

In patients taking protease inhibitors, increased bleeding (in patients with hemophilia) and diabetes/high blood sugar have occurred.

Changes in body fat have been seen in some patients receiving antiretroviral therapy. The cause and long term health effects of these conditions are not known at this time. Some patients receiving KALETRA have had large increases in triglycerides and cholesterol.

Varying degrees of cross-resistance among protease inhibitors have been observed.

The most commonly reported side effects of moderate severity are: abdominal pain, abnormal bowel movements, diarrhea, feeling weak or tired, headache, and nausea. Children taking KALETRA may sometimes get a skin rash. This is not a complete list of reported side effects.

Diarrhea may be more common in patients taking KALETRA capsules once daily compared to the twice-daily dose (57% vs. 35% of mild to severe events and possibly related to the drug; and 16% vs. 5% of events of at least moderate severity and possibly related to the drug as found in a clinical study).

KALETRA oral solution contains alcohol.

KALETRA tablets should be stored at room temperature. Exposure of this product to high humidity outside the original container for longer than 2 weeks is not recommended.

Refrigerated KALETRA oral solution remains stable until the expiration date printed on the label. If stored at room temperature up to 77°F (25°C), KALETRA oral solution should be used within 2 months.

Avoid exposure to excessive heat.

KALETRA® (lopinavir/ritonavir) tablets

[1]KALETRA Prescribing Information, October 2005

Please see important patient information on adjacent page.

1-866-KALETRA (525-3872)

CONSUMER BRIEF SUMMARY CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

KALETRA®

(lopinavir/ritonavir) tablets
(lopinavir/ritonavir) oral solution

ALERT: Find out about medicines that should NOT be taken with KALETRA. Please also read the section "MEDICINES YOU SHOULD NOT TAKE WITH KALETRA."

PATIENT INFORMATION

KALETRA® (kuh-LEE-tra)

Generic Name: lopinavir/ritonavir (lop-IN-uh-veer/rit-ON-uh-veer)

Read this leaflet carefully before you start taking KALETRA. Also, read it each time you get your KALETRA prescription refilled, in case something has changed. This information does not take the place of talking with your doctor when you start this medicine and at check ups. Ask your doctor if you have any questions about KALETRA.

Before taking your medicine, make sure you have received the correct medicine. Compare the name above with the name on your bottle and the appearance of your medicine with the description provided below. Contact your pharmacist immediately if you believe a dispensing error has occurred.

What is KALETRA and how does it work?

KALETRA is a combination of two medicines. They are lopinavir and ritonavir. KALETRA is a type of medicine called an HIV (human immunodeficiency virus) protease (PRO-tee-ase) inhibitor. KALETRA is always used in combination with other anti-HIV medicines to treat people with human immunodeficiency virus (HIV) infection. KALETRA is for adults and for children age 6 months and older.

HIV infection destroys CD4 (T) cells, which are important to the immune system. After a large number of T cells are destroyed, acquired immune deficiency syndrome (AIDS) develops.

KALETRA blocks HIV protease, a chemical which is needed for HIV to multiply. KALETRA reduces the amount of HIV in your blood and increases the number of T cells. Reducing the amount of HIV in the blood reduces the chance of death or infections that happen when your immune system is weak (opportunistic infections).

Does KALETRA cure HIV or AIDS?

KALETRA does not cure HIV infection or AIDS. The long-term effects of KALETRA are not known at this time. People taking KALETRA may still get opportunistic infections or other conditions that happen with HIV infection. Some of these conditions are pneumonia, herpes virus infections, and *Mycobacterium avium complex* (MAC) infections.

Does KALETRA reduce the risk of passing HIV to others?

KALETRA does not reduce the risk of passing HIV to others through sexual contact or blood contamination. Continue to practice safe sex and do not use or share dirty needles.

How should I take KALETRA?

- You should stay under a doctor's care when taking KALETRA. Do not change your treatment or stop treatment without first talking with your doctor.
- You must take KALETRA every day exactly as your doctor prescribed it. The dose of KALETRA may be different for you than for other patients. Follow the directions from your doctor, exactly as written on the label.
- Dosing in adults (including children 12 years of age and older):

The usual dose for adults is 2 tablets (400/100 mg) or 5.0 mL of the oral solution twice a day (morning and night), in combination with other anti-HIV medicines.

The doctor may prescribe KALETRA as 4 tablets or 10.0 mL of oral solution (800/200 mg) once-daily in combination with other anti-HIV medicines for some patients who have not taken anti-HIV medications in the past.

- KALETRA tablets should be swallowed whole and not chewed, broken, or crushed.
- KALETRA tablets can be taken with or without food.
- Dosing in children from 6 months to 12 years of age:

Children from 6 months to 12 years of age can also take KALETRA. The child's doctor will decide the right dose based on the child's weight.

- Take KALETRA oral solution with food to help it work better.
- Do not change your dose or stop taking KALETRA without first talking with your doctor.
- When your KALETRA supply starts to run low, get more from your doctor or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is stopped for even a short time. The virus may develop resistance to KALETRA and become harder to treat.
- Be sure to set up a schedule and follow it carefully.
- Only take medicine that has been prescribed specifically for you. Do not give KALETRA to others or take medicine prescribed for someone else.

What should I do if I miss a dose of KALETRA?

It is important that you do not miss any doses. If you miss a dose of KALETRA, take it as soon as possible and then take your next scheduled dose at its regular time. If it is almost time for your next dose, do not take the missed dose. Wait and take the next dose at the regular time. Do not double the next dose.

What happens if I take too much KALETRA?

If you suspect that you took more than the prescribed dose of this medicine, contact your local poison control center or emergency room immediately.

As with all prescription medicines, KALETRA should be kept out of the reach of young children. KALETRA liquid contains a large amount of alcohol. If a toddler or young child accidentally drinks more than the recommended dose of KALETRA, it could make him/her sick from too much alcohol. Contact your local poison control center or emergency room immediately if this happens.

Who should not take KALETRA?

Together with your doctor, you need to decide whether KALETRA is right for you.

- Do not take KALETRA if you are taking certain medicines. These could cause serious side effects that could cause death. Before you take KALETRA, you must tell your doctor about all the medicines you are taking or are planning to take. These include other prescription and non-prescription medicines and herbal supplements.

For more information about medicines you should not take with KALETRA, please read the section titled "MEDICINES YOU SHOULD NOT TAKE WITH KALETRA."

- Do not take KALETRA if you have an allergy to KALETRA or any of its ingredients, including ritonavir or lopinavir.

Can I take KALETRA with other medications?*

KALETRA may interact with other medicines, including those you take without a prescription. You must tell your doctor about all the medicines you are taking or planning to take before you take KALETRA.

MEDICINES YOU SHOULD NOT TAKE WITH KALETRA:

- Do not take the following medicines with KALETRA because they can cause serious problems or death if taken with KALETRA.
- Dihydroergotamine, ergonovine, ergotamine and methylergonovine such as Cafergot®, Migranal® D.H.E. 45®, Ergotrate Maleate, Methergine, and others
- Halcion® (triazolam)
- Hismanal® (astemizole)
- Orap® (pimozide)
- Propulsid® (cisapride)
- Seldane® (terfenadine)
- Versed® (midazolam)
- Do not take KALETRA with rifampin, also known as Rimactane®, Rifadin®, Rifater®, or Rifamate®. Rifampin may lower the amount of KALETRA in your blood and make it less effective.
- Do not take KALETRA with St. John's wort (hypericum perforatum), an herbal product sold as a dietary supplement, or products containing St. John's wort. Talk with your doctor if you are taking or planning to take St. John's wort. Taking St. John's wort may decrease KALETRA levels and lead to increased viral load and possible resistance to KALETRA or cross-resistance to other anti-HIV medicines.
- Do not take KALETRA with the cholesterol-lowering medicines Mevacor® (lovastatin) or Zocor® (simvastatin) because of possible serious reactions. There is also an increased risk of drug interactions between KALETRA and Lipitor® (atorvastatin); talk to your doctor before you take any of these cholesterol-reducing medicines with KALETRA.

Medicines that require dosage adjustments:

It is possible that your doctor may need to increase or decrease the dose of other medicines when you are also taking KALETRA. Remember to tell your doctor all medicines you are taking or plan to take.

Before you take Viagra® (sildenafil), Cialis® (tadalafil), or Levitra® (vardenafil) with KALETRA, talk to your doctor about problems these two medicines can cause when taken together. You may get increased side effects of VIAGRA, CIALIS, or LEVITRA such as low blood pressure, vision changes, and penis erection lasting more than 4 hours. If an erection lasts longer than 4 hours, get medical help right away to avoid permanent damage to your penis. Your doctor can explain these symptoms to you.

- If you are taking oral contraceptives ("the pill") or the contraceptive patch to prevent pregnancy, you should use an additional or different type of contraception since KALETRA may reduce the effectiveness of oral or patch contraceptives.
- Efavirenz (Sustiva‰), nevirapine (Viramune®), Agenerase (amprenavir) and Viracept (nelfinavir) may lower the amount of KALETRA in your blood. Your doctor may increase your dose of KALETRA if you are also taking efavirenz, nevirapine, amprenavir or nelfinavir. KALETRA should not be taken once-daily with these medicines.
- If you are taking Mycobutin® (rifabutin), your doctor will lower the dose of Mycobutin.
- **A change in therapy should be considered if you are taking KALETRA with:**
  - Phenobarbital
  - Phenytoin (Dilantin® and others)
  - Carbamazepine (Tegretol® and others)

These medicines may lower the amount of KALETRA in your blood and make it less effective. KALETRA should not be taken once-daily with these medicines.

- If you are taking or before you begin using inhaled Flonase® (fluticasone propionate) talk to your doctor about problems these two medicines may cause when taken together. Your doctor may choose not to keep you on inhaled Flonase®.
- **Other Special Considerations:**

KALETRA oral solution contains alcohol. Talk with your doctor if you are taking or planning to take metronidazole or disulfiram. Severe nausea and vomiting can occur.

- **If you are taking both didanosine (Videx®) and KALETRA:**

Didanosine (Videx®) can be taken at the same time as KALETRA tablets without food. Didanosine (Videx®) should be taken one hour before or two hours after KALETRA oral solution.

What are the possible side effects of KALETRA?

- This list of side effects is **not** complete. If you have questions about side effects, ask your doctor, nurse, or pharmacist. You should report any new or continuing symptoms to your doctor right away. Your doctor may be able to help you manage these side effects.
- The most commonly reported side effects of moderate severity that are thought to be drug related are: abdominal pain, abnormal stools (bowel movements), diarrhea, feeling weak/tired, headache, and nausea. Children taking KALETRA may sometimes get a skin rash.
- Blood tests in patients taking KALETRA may show possible liver problems. People with liver disease such as Hepatitis B and Hepatitis C who take KALETRA may have worsening liver disease. Liver problems including death have occurred in patients taking KALETRA. In studies, it is unclear if KALETRA caused these liver problems because some patients had other illnesses or were taking other medicines.
- Some patients taking KALETRA can develop serious problems with their pancreas (pancreatitis), which may cause death. You have a higher chance of having pancreatitis if you have had it before. Tell your doctor if you have nausea, vomiting, or abdominal pain. These may be signs of pancreatitis.
- Some patients have large increases in triglycerides and cholesterol. The long-term chance of getting complications such as heart attacks or stroke due to increases in triglycerides and cholesterol caused by protease inhibitors is not known at this time.
- Diabetes and high blood sugar (hyperglycemia) occur in patients taking protease inhibitors such as KALETRA. Some patients had diabetes before starting protease inhibitors, others did not. Some patients need changes in their diabetes medicine. Others needed new diabetes medicine.
- Changes in body fat have been seen in some patients taking antiretroviral therapy. These changes may include increased amount of fat in the upper back and neck ("buffalo hump"), breast, and around the trunk. Loss of fat from the legs, arms and face may also happen. The cause and long term health effects of these conditions are not known at this time.
- Some patients with hemophilia have increased bleeding with protease inhibitors.
- There have been other side effects in patients taking KALETRA. However, these side effects may have been due to other medicines that patients were taking or to the illness itself. Some of these side effects can be serious.

What should I tell my doctor before taking KALETRA?

- *If you are pregnant or planning to become pregnant:* The effects of KALETRA on pregnant women or their unborn babies are not known.
- *If you are breast-feeding:* Do not breast-feed if you are taking KALETRA. You should not breast-feed if you have HIV. If you are a woman who has or will have a baby, talk with your doctor about the best way to feed your baby. You should be aware that if your baby does not already have HIV, there is a chance that HIV can be transmitted through breast- feeding.
- *If you have liver problems:* If you have liver problems or are infected with Hepatitis B or Hepatitis C, you should tell your doctor before taking KALETRA.
- *If you have diabetes:* Some people taking protease inhibitors develop new or more serious diabetes or high blood sugar. Tell your doctor if you have diabetes or an increase in thirst or frequent urination.
- *If you have hemophilia:* Patients taking KALETRA may have increased bleeding.

How do I store KALETRA?

- Keep KALETRA and all other medicines out of the reach of children.
- KALETRA tablets should be stored at room temperature. Exposure of Kaletra tablets to high humidity outside the original container for longer than 2 weeks is not recommended.
- Refrigerated KALETRA oral solution remains stable until the expiration date printed on the label. If stored at room temperature up to 77°F (25°C), KALETRA oral solution should be used within 2 months.
- Avoid exposure to excessive heat.

Do not keep medicine that is out of date or that you no longer need. Be sure that if you throw any medicine away, it is out of the reach of children.

General advice about prescription medicines:

Talk to your doctor or other health care provider if you have any questions about this medicine or your condition. Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. If you have any concerns about this medicine, ask your doctor. Your doctor or pharmacist can give you information about this medicine that was written for health care professionals. Do not use this medicine for a condition for which it was not prescribed. Do not share this medicine with other people.

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The Importance of Being Earnest

Specific advantages and new treatment options for the un-undetectable

by Daniel S. Berger, M.D.

Are you someone on HIV treatment, but depressed about not being suppressed? In other words, is your viral load not undetectable? Are you uncertain about whether something can or should be done about this predicament?

For starters, let's review some background information and research. In plain English, if the virus is replicating while on treatment, it is mutating. Mutations are changes in the viral gene that allow it to continue reproducing itself and surviving. This occurs because the virus overcomes the presence of antiviral drugs in the bloodstream.

Several studies have been completed studying patients who are not undetectable with persistent or elevated viral loads. All have shown that these individuals are at risk for development of further increases in mutations to antivirals in the various drug classes.

As far back as 1998, Dr. Doug Richman reported on more than 1,000 blood samples taken randomly from the representative 132,500 patients who received care in the year 1996. This blood work was from study participants who were not undetectable or whose viral loads (HIV-RNA) were greater than 500 copies/mL in 1998.

Shockingly, 76% had resistance mutations for at least one of the drug classes and 48% of patients at that early year had already harbored resistance mutations to two drug classes. Additionally, 41% had resistance mutations to protease inhibitors, and 13% in 1998 had already developed triple class resistance mutations.

Thus, we can imagine what the statistics would look like today, with many more years of treatment and exposure to more medications by most patients. Let's not forget about the many individuals now seroconverting or those getting infected with resistant virus at the starting gate.

Last year's Conference on Retroviruses and Opportunistic Infections highlighted the SCOPE study investigating the changes in people on treatment with viral loads greater than 1,000 copies. They deferred regimen changes during the observation period of the study, with resistance testing every 120 days. At the end of one year, 44% had at least one new resistance mutation to one class; 23% to a nucleoside analogue, and 18% to a protease inhibitor. Thus, persistent viremia—that is, detectable virus—runs the risk of possibly limiting future treatment options. I should also mention that two other studies had similar results.

With these facts in mind, let's discuss an example of managing a patient in this situation. Justin is a treatment-experienced guy who is failing his current antiretroviral regimen. He was on treatment for a few years now and his latest CD4 T-cell count is 290 cells/mm3, which has been relatively stable over the last year. His last visit with his doctor showed a viral load of 4,500 copies/mL, but this has been slowly increasing over the past few months. As a physician, it should be possible to construct a more effective treatment for Justin.

The doctor's discussion with Justin would probably include answering questions about when to switch to the next treatment. Should Justin wait for his T-cell count to begin dropping? Should we wait until his viral load goes above 10,000? Should we wait until Justin starts feeling tired or sick, since currently he feels pretty well, although he is on testosterone injections at the clinic? Should we wait until he has better treatment options, since he has already failed Kaletra and also had a history of Viramune? Justin probably has mutations in several classes of drugs.

The answer to these questions should be *NO*! We don't wait for patients to get sick, nor deteriorate. We try to be preemptive and offer patients more options and hope for the future.

Accordingly, there may be treatment options based on resistance testing, but other new drugs from newer classes can provide greater possibilities. Justin's doctor may not know about the availability of MK-0518 (the Merck integrase inhibitor), or TMC-125, a second generation non-nuke. Educate him!

Nor may his doctor be involved in research that can grant possible access to Gilead's integrase inhibitor, GS 9137. However, Prezista is a newer protease inhibitor shown to be effective for resistance to other PIs, and Fuzeon is an injectable fusion inhibitor. Both are readily available in your local drug store or AIDS Drug Assistance Program (ADAP) formulary. Other older agents may also show benefit, such as Ziagen and/or Viread.

Justin should have a resistance test to inform his options. A genotypic test examines the unique gene sequence of Justin's virus, mapping out any expected resistance; a phenotype test provides clinical resistance information about which drugs Justin's virus is susceptible to or effective.

The risk of waiting is that Justin will continue to develop more resistance and see his options diminish. Perhaps now, having been exposed to one protease inhibitor, he may not have accumulated overwhelming resistance mutations to PIs and may have several other PIs as options. Finally, newer treatments are under study and their availability provides patients with new hope and improved quality of life.

Daniel S. Berger, M.D., is Medical Director of Chicago's largest private HIV treatment and research center, NorthStar Healthcare. Dr. Berger can be reached at DSBergerMD@aol.com or (773) 296–2400.

A People Who Once Were

by Keith R. Green

"I am afraid that there will come a time when history books refer to African Americans as a race of people who once were."—*Saundra Johnson, community educator and long-time HIV/AIDS advocate*

Early on the last morning of 2006, two masked gunmen entered the basement of a two-flat building on Chicago's South Side. The first floor residents of the building were hosting a party that was just about to end. They were known to be gay. They were also known to frequently host rowdy late night parties that lingered into the wee hours of the morning. On more than one occasion, according to some reports, the police have been called in to respond to a myriad of offences—ranging from disturbing the peace to aggravated battery.

Local news reporters who followed the story interviewed a number of neighborhood residents. From their perspective, this was bound to happen. The people in the "gay" house had been warned that "this type of activity" was not acceptable in "this type of neighborhood." They had been told to move it and to take it back to the suburbs. They had not adhered to the warnings.

The gunmen said no words—they simply sprayed into the crowd. The Chicago Police Department concluded that there was not enough evidence to investigate this tragedy as a hate crime. The gay community became outraged. Outraged at the way that they felt the investigation was being handled. Outraged at the Department's insensitivity as it relates to constant threats of homophobia, particularly in this neighborhood. Outraged at the blatantly homophobic remarks made by community members. Outraged that black "leaders" such as Jesse Jackson or James Meeks did not publicly speak out about the shooting, one way or the other. And outraged at each other for not knowing how to respond.

A community forum was hosted at a local gay-owned restaurant and, on the day that this country acknowledged the birth of Dr. Martin Luther King, Jr., a march for "peace and respect" was held through the streets of the affected neighborhood. Black and white, gay and straight, people from all over the city came out to show their support for the GLBT residents of this community—who live their daily lives in a sea of intolerance.

While I have been both present at and fascinated with the community response, I have also been overwhelmed with the feeling that we are all somehow missing the bigger picture. From the very beginning, rumors began circulating that the circumstances around this event may not have been what they appeared to be. The degree of community homophobia was undeniable, as evidenced by the remarks made from the neighborhood thugs to the first news reporters on the scene. But the word on the street was that the shooting stemmed from a dispute that had occurred earlier in the night between partygoers and did not in any way meet the legal qualifications of a hate crime.

The bigger picture, then, looks like the acclimation of violence in black communities all over the world. We have become so familiar with these kinds of horrific events occurring within our communities and neighborhoods that unless buzz of "hate crime" surrounds them, we don't look up from our daily lives to pay it any attention. If we did, we would probably become overwhelmed. And maybe that's what needs to occur. Maybe we need to become so overwhelmed with all that is really happening in our community that we become forced to do something about it.

But there would just be too much to do now, wouldn't there? If we paid attention to the disproportionate number of us who are behind bars or infected with HIV. If we looked at how the crack cocaine epidemic has further burdened our urban ghettos and poverty-ridden slums. If we paid attention to the number of us who earn college degrees (or high school diplomas for that matter) compared to other races of people in this country. Or how our youth perform on standardized school exams in comparison to other children their age. If we really paid attention to any of the social ills that face Black people today, there would be just too much to do. And maybe that's why so many of us have resorted to doing nothing.

While I've argued Saundra Johnson up and down since I heard her utter those dismal words nearly two years ago, it's hard to deny the fact that her hypothesis may have some validity. The daily news provides all the supporting evidence that she needs.

Community forums and marches are a wonderful start, but I'm afraid that if we are to actualize a different outcome than predicted by Saundra, there is something else that we must do. We must effect change in the very fabric of our world. And the issues of our world are not just limited to GLBT issues or black issues or HIV issues. No. It's about universal *human* issues. Every human should feel safe where they live—wherever they live. Every human should have access to a good education and life-saving medications. Every human should have the right to life, liberty and the pursuit of happiness. Until we all do, none of these luxuries are guaranteed to any of us.

And that's cause for *all* of us to pay attention.

Photo © Russell McGonagle

The Burning Bowl

An Rx for the spiritual health of the AIDS advocacy movement

by Jim Pickett

On the day of New Year's Eve, I was blessed to connect with Unity in Chicago, part of the Association of Unity Churches (see unity.org.) A spiritual movement free of discrimination on the basis of race, gender, age, creed, religion, national origin, ethnicity, physical disability, or sexual orientation, Unity follows these five basic tenets:

- There is only one Presence and one Power, God.
- God is present in all people as divine essence, our Christ nature.
- We create reality through thoughts held in mind. This is the spiritual law of mind action.
- Through prayer and meditation, we align our heart-mind in God.
- We commit to the practical application of these principles in our daily lives.

It is a fantastic, loving movement dedicated to peace, love and understanding without dogma, drama or fundamentalism.

The love of my life brought me to Unity on that day, after years of my being relatively adrift in my spiritual quest. I have always believed in the immense power and infinite wisdom of the universe and the truths inherent in all the world's religions. I have reaped the rewards of the universe while synchronous with its guidance, and experienced the pain indicative of being in its shadow. Much of my struggle came from attachment to negative thoughts and energy.

The Burning Bowl ceremony, which took place that day, so simple and so beautiful, continues to resonate with me. The service consisted of writing down the things/issues/thoughts/feelings/hurts that no longer serve your purpose, and hold you back from the wisdom and the compassionate love that is part of every one of us. The list could be as short or long as needed. As the paper touched the flames, and all those words became ashes, you began to release this ponderous baggage from your life.

I wept like a baby. The healing I experienced through this meditative exercise set my course for the year and, I pray, for the rest of my life. I felt 20 pounds lighter.

It occurs to me that there are at least three things we, as a national AIDS advocacy movement, could and should release into the fire.

1. Ego. Sadly, so much of our work becomes defined by unbridled ego, self-aggrandizement, drama, and by turf, not defined by the real needs of people living with and at risk for HIV/AIDS. When AIDS advocacy is about personalities, AIDS advocacy has lost its way. We are serving no one but ourselves, and untold numbers are hurt in the process. And our credibility is threaded through those ruins. Burn, ego, burn.

2. Division. Time and again we fall into traps that seek to divide us, people living with and at risk for HIV/AIDS, by geography, by gender, race, age, sexual behavior and identity, by mode of transmission, by the "good" and the "bad", by those who "deserve" assistance and those who somehow, do not. Why must we bash one group to advocate for another? Why does fighting for one area of the country mean we stridently declare another area should get less? Why must every equation have winners and losers, when it comes to the PEOPLE we are fighting for? Divided, we forget this basic truth. Division to the flames.

3. Fear. Fear keeps us from speaking truth to power when it really matters, and leaves us, people living with and at risk for HIV/AIDS in the lurch; fear keeps us at the margins, tinkering with the not-so-significant policy minutiae while actively not seeing the big picture and defining in clear terms what is really needed. Fear allows us to dismiss the other, whoever that other may be, and fear keeps us ignorant and reactive, instead of open, wise, and visionary. Fear says its okay to not talk about sex and drugs, fear gives an excuse to dismiss gay men and injection drug users and sex workers. Fear says we can't say "anal intercourse" or "transsexual" or "needle exchange" or "comprehensive sex education." Fear accepts abstinence-only money. Fear deposits us on a desert island with no fresh running water, fences us in, and shuts us down. Fear relies on simplistic fixes to complex problems—like the idea of testing everybody and their little sister as THE answer to HIV prevention. Fear removes people's human rights, and fear impedes access to the knowledge that is critical for survival in these difficult and challenging times. Fear is fundamentalist and dogmatic. Fear to ashes.

None of this will come easy. Nothing of any consequence is. In this country, there are over a million people counting on us, and countless millions more across the globe, who also know it ain't easy.

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