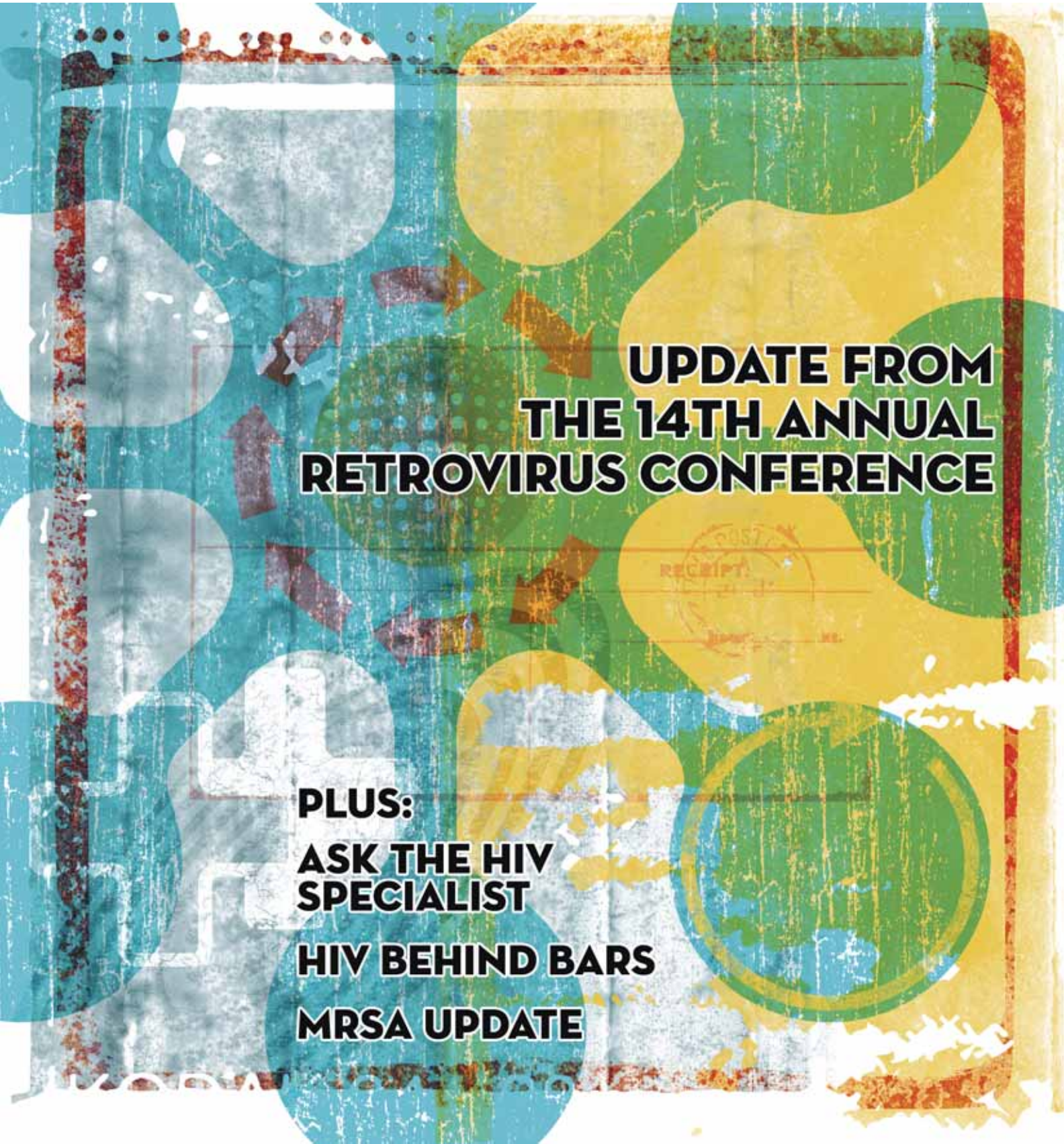
May / June 2007

Positively Aware

The Journal of Test Positive Aware Network



UPDATE FROM THE 14TH ANNUAL RETROVIRUS CONFERENCE

PLUS:

ASK THE HIV SPECIALIST

HIV BEHIND BARS

MRSA UPDATE

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

SF-B0001B-07-06

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May / June 2007
Volume 18 Number 3

Departments

Articles

Articles continued

14th Annual Retrovirus Conference (CROI) continued

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

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

Programs and Meetings

Programs and Meetings at TPAN

- Support Groups
- Rapid HIV Testing
- Yoga, Reiki and Massage
- Needle Exchange Program
- Buddy Program
- Access Medical Clinic at TPAN
- PULSE, an HIV-positive Weekly Social
- TEAM (Treatment Education Advocacy Management)
- Positively Wired—A Free Basic Computer Skills Workshop
- Positively Aware Party at Hydrate
- SMART Sexx
- TRADE (Teachin', Reachin', Advocatin', Demonstratin', Empowerin')

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

test positive aware NETWORK

Test Positive Aware Network
5537 North Broadway
Chicago, IL 60640

phone: (773) 989-9400
fax: (773) 989-9494
e-mail: tpan@tpan.com
http://www.tpan.com

Editor
Jeff Berry

Associate Editors
Keith R. Green
Enid Vázquez

Executive Director
Rick Bejlovec

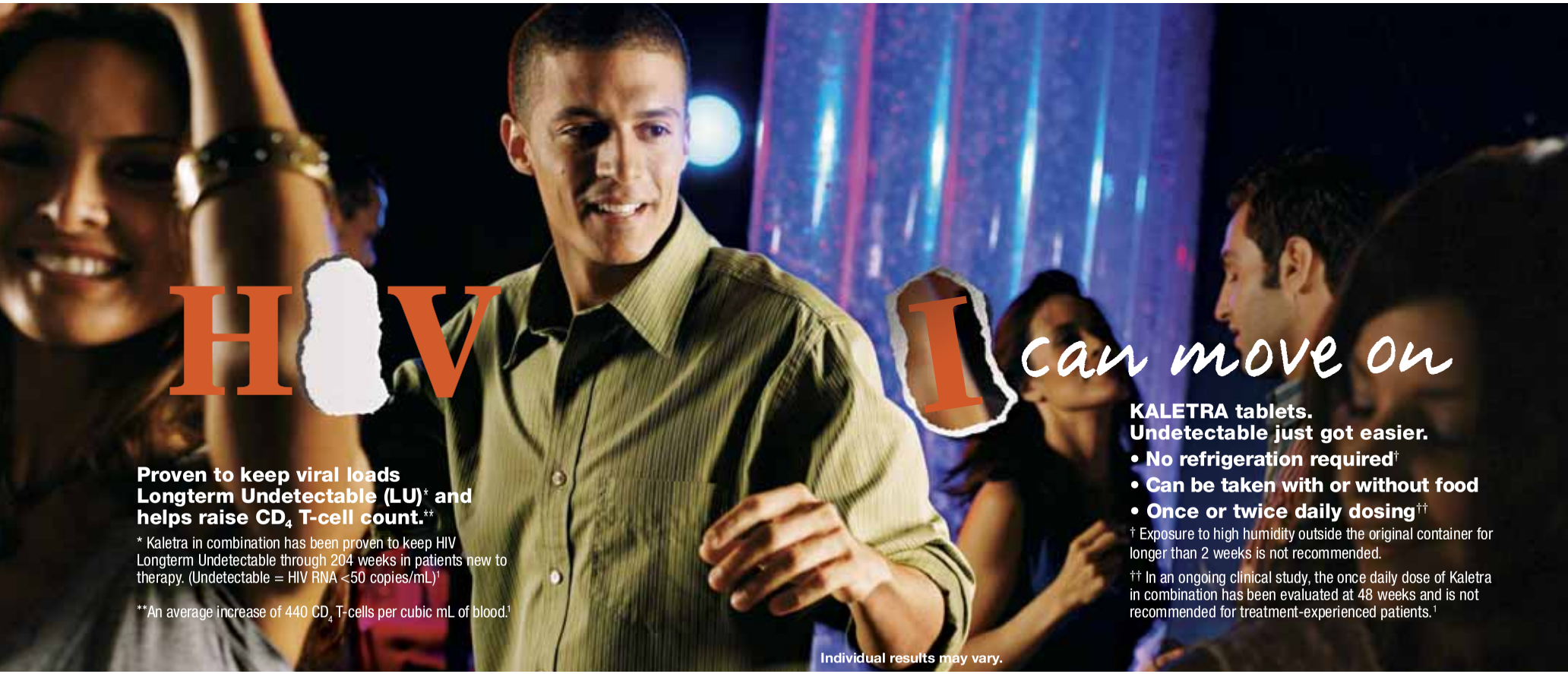
Director of Education and Advocacy
Matt Sharp

Director of Advertising
Danny Kopelson

Contributing Writers
Laura Jones, James Learned, Jim Pickett, Sue Saltmarsh

Medical Advisory Board
Daniel S. Berger, MD, Patrick G. Clay, Pharm.D., Rupali Jain, Pharm.D., and Ross M. Slotten, MD

Art Direction
Russell McGonagle



Kaletra 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.

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 if you 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 methylergonovine 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®, 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.

KALETRA®
(lopinavir/ritonavir) tablets

ASK YOUR DOCTOR TODAY

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 at least moderate severity and possibly related to the drug as found in a clinical study).

KALETRA oral solution contains alcohol.

[1]Kaletra Prescribing Information.

Please see important patient information on adjacent page.

1-866-KALETRA (525-3872)

KALETRA.COM

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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North Chicago, IL 60064, U.S.A.

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The Here and Now

I'm grateful for unfunded needle-exchange programs. I'm grateful for volunteers who give because they can. I'm grateful to be able to do work that I am passionate about. I'm grateful to come to the office everyday and be with a diverse group of talented, bright, innovative, and crazy individuals. I am grateful.

I'm grateful that there are people who aren't in it for the money. I'm grateful for people such as Bono who go after the money. I'm grateful for Doctor's without Borders. I'm grateful for the nurses and doctors who stay to work in Africa, and aren't siphoned off by the "brain-drain." I am grateful.

I'm grateful for TPAN, for ACT-UP, for ATAC, for ECAB, for TAC, and for TAG. I'm grateful for the CDC, the FDA, the NCAB of the ACTG, and WHO. I'm grateful for ART, for PAPs, for PEP, for PrEP, for AZT, 3TC, d4T, and for New-Fill. I am grateful.

I'm grateful to have wonderful, life-long friends. I'm grateful for the friends that I have lost. I'm grateful to have a family who loves and believes in me. I'm grateful for Stephen, the love of my life. I'm grateful for my cats, who are my kids. I'm grateful for my health, my doctor, my surgeon, and my pharmacist. I'm grateful for Ramona, because when she draws my blood it never hurts. I am grateful.

I'm grateful for all the people who have entered clinical trials. I'm grateful for a board of directors who give selflessly of their time for a cause they believe in. I'm grateful for clients who smile and say hello when I walk by them in the hallway. I'm grateful to our donors. I'm grateful for such amazing writers who contribute to our magazine. I'm grateful to those who review our articles for us. I'm grateful for our readers. I'm grateful for everyone who responds to our surveys. I am grateful.

I'm grateful to my mom and dad for teaching me about life. I'm grateful for my past. I'm grateful for childhood memories that still make me laugh. I'm grateful for my grandmother who lived to be 102. I'm grateful for the life lessons, the joy, the heartache, the pain, and for my therapist. I'm grateful to be a survivor. I am grateful.

I'm grateful for my triglycerides, my blood pressure, my cholesterol and for Lipitor. I'm grateful to be on meds that have side effects that I can live with. I'm grateful for Imodium. I'm grateful for adult diapers and for sitz baths. I'm grateful that I have now become my parents, and can sit around with my family or friends and we can talk about our ailments and recent surgeries. I'm grateful for antiretrovirals, for antibiotics, for antidepressants and for Auntie Mame. I am grateful.

I'm grateful for support groups that made me realize I was not alone. I'm grateful for the little voice inside me. I'm grateful when I listen to it. I'm grateful to be able to forgive. I'm grateful when I am forgiven. I'm grateful for faith, hope and dreams. I am grateful.

I'm grateful when I can let go of fear. I'm grateful to have choices. I'm grateful for challenges and conflicts that arise in my life, and for the opportunities for growth and learning that they offer. I am grateful.

I'm grateful to be able to take joy in my accomplishments. I'm grateful to be able to admit when I've made a mistake. I'm grateful to be human. I'm grateful to be HIV-positive. I'm grateful to still be here.

I am so grateful.

Jeff Berry
Editor
publications@tpan.com

Readers Forum

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Write to: *Positively Aware*,
5537 North Broadway
Chicago, IL 60640
Fax: (773) 989–9494
E-mail: readersforum@tpan.com

Banishing chipmunk cheeks

Editor's note: A reader of HCV/HIV Today *wrote the following comment to that publication following a reprint of "Banishing Chipmunk Cheeks and Bullfrog Neck" [September/October 2006]: As a survivor of oral cancer, I know that maxillofacial radiation therapy causes soft teeth and dental caries. Most of this happens 20 years post-treatment, so patients have to balance risks and benefits—as usual. The article suggests that radiation is appropriate, as opposed to surgery, but the attendant issues are more complicated than that.*

"Myths"

I had a very upsetting phone conversation with my daughter the other day. She is pursuing a degree in Acupuncture and Oriental Medicine, and had just gotten out of a class where the instructor covered the topic of HIV/AIDS. The teacher espoused his personal view that HIV does not cause AIDS, and directed the students to a website that tries to discredit what it calls "myths" relating to the virus: www.virusmyth.net. She was very eager to share this news with me, but it was almost like listening to someone excitedly tell me that the Holocaust never happened or that they just found out that Evolution is just a theory. I got very upset with her, and the conversation ended badly.

I am trying to be an open-minded dad, but since I am living with the virus and see what it is doing in my own body, and have seen what it has done to many friends over the years, I am having a very difficult time not being defensive over what some very credible scientists are proclaiming on this website. Can you help me get to the truth, and sort out what are facts versus what are myths?

Dan in Chicago, via the Internet

Editor's note: Visit the Treatment Action Campaign website at http://www.tac.org.za/debunking.html for excellent information on this topic.

When Opposites Attract

Many thanks to Keith Green for his article on serodiscordant relationships ["When Opposites Attract," March/April issue].

I too am in one. My partner and I were tested six months after my moving in. We recently stopped using condoms and I felt uncomfortable not knowing each other's current status. The one thing we did before getting tested was to sit down and have a heart-to-heart about what it would mean if we both were no longer negative. We decided to stay together no matter the outcome. As it turns out, his test came back positive. He took it very well, I cried on and off for a week. The two things that helped were the "pre" discussion (so the only thing left was to make it work), and discussing safer sex practices with a professional. Fortunately we live in a large city with an excellent GLBT clinic. At the time he was on a city-appointed HIV/AIDS committee and I was working for an agency assisting HIV-positive people. Between the two of us, we should have known the best way to have safer sex, but there was a lot that we didn't know. Some things we did are considered risky (used his semen as lube during masturbation) and fisting without gloves. Even in this article I learned that penis to penis sex is considered riskier that anal sex with a condom.

The person inside was far more important to me for our relationship to last forever than the inconvenience of having to put on the occasional condom. It's been four years and his brain is the sexiest organ I have ever found.

Marc, Houston, Texas, via the Internet

I have a question about the article "When Opposites Attract" in the March/April 2007 edition of Positively Aware. In the sidebar to the article entitled "Dr. Bell's Safer Sex Spectrum," in the Male/Male sexual risks column, "oral sex without a condom/dental dam" is listed as riskier than both anal receptive and anal insertive sex, as well as "penis to penis sex."

As an HIV prevention educator with a major hospital network, I am concerned that this information conflicts with other current information. I was wondering if someone there could support this information or offer sources which can support this risk assessment. As our prevention work with at-risk men follows a harm reduction model, our HIV counseling, by your chart, is actually increasing risk.

Lew Alessio, Men's Health Educator, just guys—the men's HIV Prevention Program at MaineGeneral Health, Augusta, Maine

Dr. Bell responds: Please note that the references for transmission are for STIs (STDs) and HIV. Using barrier methods with any sex act (versus unprotected sex, be it oral, anal or vaginal sex) makes it safer. Remember, STIs can be transmitted via body fluid and/or some via skin-to-skin contact.

Editor's note: "Condom use" always implies "correct condom use." Using a poorly-rated condom will increase the risk of condom failure. Always remember to use a water-based lube with latex condoms, as oil-based lubes will cause latex to disintegrate. And if the condom falls off or breaks during sex, the risk obviously increases.

Anal HPV

I appreciated this article [Surviving Anal Cancer, May/June 2004]. I am an HIV-negative, straight woman recently diagnosed with HPV anal polyps after my

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

routine, after 50, colonoscopy. My MD was surprised to find out that it was HPV and recommended a sigmoidoscopy in a year. Even though I have been a Registered Nurse for years it did not register how dangerous HPV was until all the recent advertisements for the vaccine.

Within a year I had developed high and moderate grade dysplasias. So I was off to surgery. My surgeon told me to come back in a year. But after much research and articles like yours, I had my first three month checkup at the University of California San Francisco (UCSF). My biopsies are pending. I don't want to go through that surgery again so I will go back to UCSF for further treatment.

I have had a normal cervical Pap smear all my life. I was married for 15 years until my husband died three years ago, and I have not been in a sexual relationship since then. I had anal sex several times in one relationship 30 years ago. I am not the norm. What is scary is there are no support groups, and no one wants to talk about it. UCSF has no support group, even among the gay community.

If I can get it anyone can. How many anal cancers are developing because women my age are not having colonoscopies? Anal Paps should be routine for everyone in my view. But then the problem is that Dr. Barry at UCSF has only trained 30 MDs in the U.S. to examine and treat the problem. I found one MD in the state of Oregon that can, but he has to take patients to the operating room, which makes the price of treatment thousands of dollars more. So few can treat, few will talk—how many are dying? How long will it take for anal HPV to be recognized? Cervical and anal tissue are very similar.

Name withheld, via the internet

Medical marijuana

I am a medical writer and need to learn more about medical marijuana. Some AIDS patients use Marinol to treat appetite loss. Marinol is relatively expensive, and I would like to know if you are aware of any company developing a generic equivalent. If you do not know, please refer me to people who might have some information about generic Marinol. Thank you for your consideration.

Elisabeth Hefti, Ph.D., *Biotech Business Link*, NY, NY, via the Internet

Pharmacist Rupali Jain replies: Marinol is only currently available in the United States as the name brand product. Depending on length of the patent of the drug, I am unsure how long it will be until it goes generic. Many companies have patient assistance programs to help with the expense of the medication for those who qualify.

Dr. Cruise Control

Hi, you have a great website. I'm going to recommend it to high school students. I'm planning a school wide Student/Parent HIV/AIDS awareness day (and praying for approval) and I would like to include the article "Dr. Cruise Control " [HIV Systems Check, Fall 2006 issue] in the handout package along with various periodicals and personal testimonies.

Alice Lang, PTA mom and Eternal Hope Community Development Corporation, Inc., East Orange, New Jersey, via the Internet

Kudos on HIV Drug Guide

I wanted to write and congratulate you on the 2007 HIV Drug Guide. I also wanted to thank you for all of the hard work you do. Every year we receive the Drug Guide and every year we need to order additional copies because it's so popular with both staff and consumers. This year's issue is, in my opinion, the best one yet. Keep up the great work! I work in an HIV Health Library and it gives me a sense of security to know that a publication as well-written, timely, and readable as *Positively Aware* is out there and available. Almost daily I find myself copying, forwarding, or referring to content from *Positively Aware*. The Drug Guide is a great beginning of the year kickoff, but the rest of the issues throughout the year are just as dazzling. Enid, Jeff, Matt and everybody else: the world wouldn't be quite as good without you.

James Apt, HIV Health Specialist, AIDS Action Committee, Boston, MA, via the Internet

HIV Drug Guide and AWP

Hello and thanks for the latest *Positively Aware* Eleventh Annual HIV Drug Guide. I actually discovered it on "The Body" website. I just have one question: You note that each drug in your guide has an AWP with the dollar amount, but was wondering what does "AWP" actually mean?

Thanks for the info!
Terry, via the internet

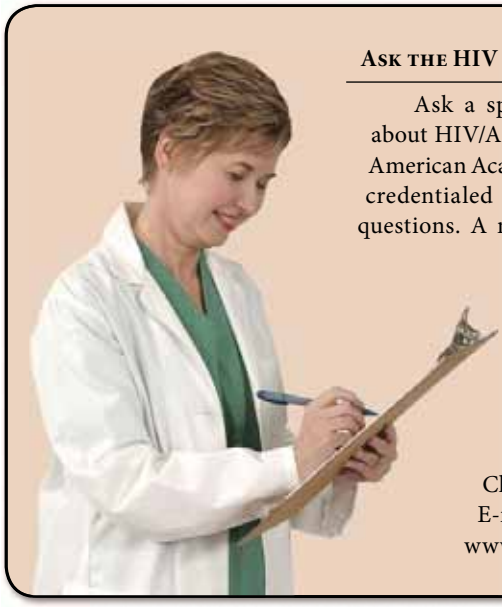
Editor's note: AWP stands for Average Wholesale Price, and is a national average of list prices charged by wholesalers to pharmacies. AWP is sometimes referred to as a "sticker price" because it is not the actual price that larger purchasers normally pay, which is often considerably lower. It is not what your insurance company will pay for the drug, or even what you would have to pay if you did not have insurance—most of the time that amount will be much higher than the AWP. AWP information is publicly available.

Youth and HIV

I especially appreciated the July/August 2006 issue of *Positively Aware*—which presents a realistic but hopeful message for and about young people. When I received a box of copies I placed some in our clinic waiting room and others in the emergency room waiting room (keeping only a few for myself). They went like hot cakes!

I will soon be speaking with high school students about HIV and STDs. Some may be HIV-infected or have a family member who is positive. Others are probably just curious. I would greatly appreciate receiving another box (25 or 50 copies) of this particular issue. Also if you have an issue which speaks to HIV rookies, that would be very helpful also. Thanks!

Barbara Lee Perlmutter, MD, Hoboken, NJ, via the Internet



Ask the HIV Specialist™

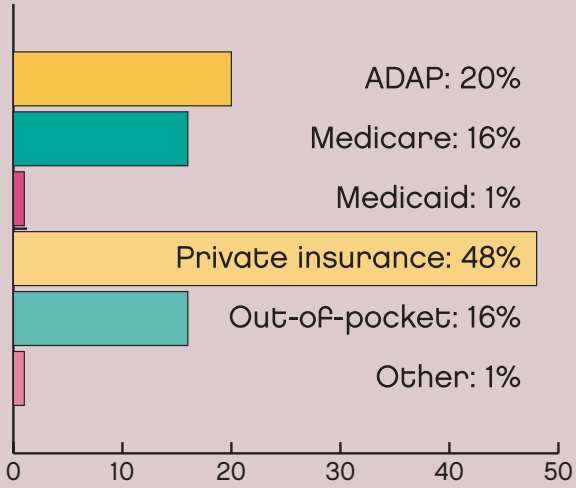
Ask a specialist questions you may have about HIV/AIDS, and HIV/AIDS treatment. An American Academy of HIV Medicine (AAHIVM) credentialed HIV Specialist will answer your questions. A new column regularly featured in *Positively Aware* magazine, in collaboration with the AAHIVM (see page 15).

Send your questions in care of
Ask the HIV Specialist™,
5537 N. Broadway,
Chicago, IL 60640
E-mail: aahivm@tpan.com or visit www.tpan.com.

March / April 2007 PA Online Poll Results

How do you pay for your HIV medications (check all that apply)?

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



March / April 2007 PA Online Poll comments

- Private insurance, and ADAP picks up the co-pays which average $50-$100 a month.
- Free through VA Medical System, however options are limited.
- Complications with "primary care provider" creates limitations for me with Medicaid. Not that Fuzeon is a drug of choice on any number (viral load, CD4) for this HIVer—geesh, keep it simple? I digress; Medicaid was reluctant to pay for Fuzeon.
- Why are the drugs so expensive? Surely there are generics available since patents are only good for seven years. What gives?
- Co-payments are killing us!

May / June 2007 PA Online Poll

Have you ever been diagnosed with MRSA (drug-resistant staph infection)?

Give your answer at www.tpan.com

Sustiva
Ad
Page Here
ftp'd to
Woodward

Sustiva
P.I.
Page Here
ftp'd to
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Does HIV make someone more susceptible?

My son is a certified medical assistant who works daily with people who are ill. He has a CD4 count of 311, and he takes no HIV meds at this time.

I am concerned because he has begun breaking out in numerous rashes on his face, neck, and chest. Last month, he became ill at the clinic where he works, nearly losing consciousness because he could not breathe. He was given erythromycin by needle, and Benedryl, then rushed to the E.R. Still, no-one knows what caused the "attack."

My son has a friend who has AIDS. Would an AIDS patient transfer something to my son that would make my son in worse condition, assuming all precautions are taken?

The short answer is no—HIV is transmitted through the exchange of bodily fluids during sexual contact with an infected person, sharing needles and syringes or other drug works with someone who is infected, during pregnancy or labor and through breast-milk of someone infected with HIV, or very rarely in the U.S. via transfusion of infected blood or blood products. It does appear to be possible for a person with HIV to become infected with a second strain of HIV through some of the ways listed above, running the risk of acquiring drug-resistant virus, for example.

It sounds like your son is doing good things for himself—working hard, keeping up with his medical care, talking with his mother... If his CD4 count is staying below 350, it is likely time to actively review the pros and cons of starting antiretroviral therapy. Other healthy behaviors include eating a balanced diet, getting enough sleep, exercising regularly, avoiding tobacco, alcohol and other drugs, and practicing safer sex (just to name a few).

Aimee Maree Wilkin, MD, MPH, AAHIVS, Wake Forest University, School of Medicine, Winston-Salem, NC

Mad about Z

I am an HIV-positive nurse and an asthmatic. When I get a cold I usually get a chest infection, so I usually get a course of Z-PAK. My current doctor advised me to take Sudafed and Tylenol instead of prescribing the antibiotics. I am hacking up gobs of yellow sputum, though, and am mad enough to switch doctors. Why when I have cold that usually leads to a secondary chest infection, would it be contraindicated to have a course of antibiotics for my chest, especially when I'm HIV-positive?

In treating what sounds like recurrent bronchitis after upper respiratory infection, data on antibiotics are controversial, and may actually suggest that they are unlikely to help. More appropriate treatment may be risk reduction behavior like reducing exposure to smoke and allergens, inhaled steroids, bronchodilators, and mucolytics.

John W. Gerwig, PA-C, AAHIVS, John Hopkins University, Baltimore, MD

HIV vs. AIDS

I need to know how you tell the difference between being HIV-positive and having full-blown AIDS. My son has told me he is HIV-positive and I am scared to death. The doctor has told him he will be taking a medication that will make him sick. He lives in Chicago, I live in Michigan and I am retired and I do not know what to do to help.

You may want to help your son seek care from an HIV Specialist™. Your son's provider may not be current with the new medications and their side effects. "HIV-positive" means that the person is infected with HIV, which affects the immune system. An AIDS diagnosis occurs when the immune system declines to a certain point (under 200 CD4 cells), or the patient develops certain illnesses, like PCP pneumonia. In my 12 years as an HIV care provider, I have seen many patients with advanced AIDS who begin treatment and do very well for many years.

I reassure all of my newly-diagnosed patients that when they need to begin HIV medications, they have excellent treatment options. We see significantly fewer side effects with new medications than we saw years ago. My patients have returned to work, completed college courses and enjoy healthy, active lives.

Your local HIV community-based organization or health department can help answer your questions. AAHIVM's "Find A Provider" search at www.aahivm.org can help you find an HIV Specialist™ in your area.

Kathryn L Hall, RN, PA-C, AAHIVS, Yellowstone City County Health Department, Billings, MT

E-mail your questions to aahivm@tpan.com, or send a letter in care of "Ask the HIV Specialist," TPAN, 5537 N. Broadway St., Chicago, IL 60640.

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.

Are you seeing an HIV Specialist™?

Finding the AAHIVM-credentialed HIV Specialist™ in your community is a click away with AAHIVM's **"Find A Provider"** search at www.aahivm.org.

The American Academy of HIV Medicine (AAHIVM)'s HIV Specialist™ credentialing program is the first and only clinical credentialing program offered domestically and internationally to physicians (MDs and DOs), nurse practitioners and physician assistants specializing in HIV care. HIV care providers become designated HIV Specialists™ (AAHIVS) after meeting experience and education requirements, and successfully completing a rigorous exam on HIV-specialized medical care.

Due to space limitations, all submitted questions cannot be answered in this column, but we are making every effort to ensure that you receive the information you have requested from the HIV Specialist™. For more information about AAHIVM, visit www.aahivm.org or call 202-659-0699.

HIV and Cancer Study Update

AIDS Malignancy Consortium opens next major HIV lymphoma trial

by Jeffrey Schouten, MD, AAHIVS

The AIDS Malignancy Consortium (AMC) is a group of a dozen major medical centers, funded by the National Cancer Institute (NCI), that conduct research in the field of HIV-related cancers. The research focuses on the three most common cancers seen in people with HIV; Kaposi's sarcoma (KS), lymphoma, and human papilloma virus (HPV)-associated anal cancer.

KS is an abnormal growth of blood vessels associated with a herpes-type virus, KS-HV or HHV-8, which most commonly appears as purple nodules on the skin. With current antiretroviral therapy (ART) the incidence of KS has declined dramatically in the past decade, but still remains a problem for many people. The AMC has several KS trials ongoing.

Lymphoma is a cancer of the lymph nodes. The most common type seen in people with HIV is non-Hodgkin's lymphoma (NHL), but increasingly Hodgkin's lymphoma (HL), which historically has had a higher cure rate with chemotherapy, is also occurring in people with HIV infection. With current ART, the overall incidence of lymphoma is declining, but not as much as the decline seen in KS. Fortunately, one of the most aggressive lymphomas, that of the brain, or CNS lymphoma, has had a more dramatic decline with ART. However, there still remains an ongoing need for clinical research into the treatment of HIV-associated lymphoma.

The AMC has conducted several large trials to study the best treatment for HIV-associated lymphoma. Trial 010 enrolled about 200 people and compared the standard chemotherapy regimen, CHOP, with CHOP plus rituximab, a monoclonal antibody that attacks lymphoma cells. Rituximab attacks a site on the surface of lymphocytes known as CD20. Most HIV-associated lymphomas have CD20 present on the lymphoma cell surfaces. Rituximab plus CHOP had already been shown to be better than CHOP alone in people with lymphoma who were HIV-negative. In the 010 study, better tumor control was evident in the rituximab treated group in terms of progression-free survival, and rate of death due to lymphoma, but the overall complete response (CR) rate was not significantly different in the two arms of the study. The results of this trial showed that the addition of rituximab improved the response to the chemotherapy. However, in people with very low CD4+ T-cell counts, fatal infections occurred more frequently with the addition of the rituximab, suggesting that people with less than 100 CD4 cells should also receive prophylactic antibiotics in addition to the rituximab with chemotherapy.

Following the 010 trial, the AMC conducted trial 034. This trial studied a chemotherapy regimen that is probably more potent than CHOP, but needs to be given as a four-day continuous infusion every three weeks, for two to six cycles, depending on response. The regimen is known as EPOCH. The study also asked the question if it is better to give the rituximab at the same time as the EPOCH chemotherapy, or afterwards. About 150 people enrolled in this trial. The results of the 034 trial were reported this past October at the International AIDS Malignancy Conference in Washington, DC. This trial showed very good response rates to the infusional regimen, and rituximab worked better when given at the same time as the chemotherapy rather than following the completion of the chemotherapy. In the group that received EPOCH and rituximab at the same time, there was a 65% CR rate and an estimated 80% one-year progression-free survival. In contrast, the group which received the rituximab after the EPCOH chemotherapy had 38% CR rate and an estimated 72% one-year progression-free survival. Also, in this trial, concurrent administration of rituximab was not associated with an increased risk of infectious death with the supportive care given and infection prophylaxis. These results show the dramatic improvements realized over the past decade in the treatment of HIV-associated lymphoma, when the average survival was initially measured in months, not years.

Building on the above results, the AMC has just opened its newest HIV-associated lymphoma trial 047. The title of this new study is "A Phase II Trial of Doxil, Rituximab, Cyclophosphamide, Vincristine, and Prednisone (DR-COP) in Patients with Newly-Diagnosed AIDS-Associated B-cell Non-Hodgkin's Lymphoma (NHL)." The purpose of this trial is to determine if a chemotherapy regimen that does not require prolonged infusion of chemotherapy drugs can result in the same high response rates seen in the 034 trial. Doxil is doxorubicin (one of the most potent drugs to treat lymphoma) encapsulated in STEALTH® liposomes. Liposomes are microscopic vesicles that encapsulate active drugs, allowing them to circulate in the body longer and be more potent. Participants will receive up to six cycles of the chemotherapy, administered every 21-26 days. A total of 40 people will be enrolled in this trial.

This trial, like the earlier AMC trials, will potentially have a significant impact on the treatment of HIV-associated lymphoma. If the results of the 047 trial are found to be similar to those reported for the 034 trial, the AMC plans to continue forward with a larger randomized trial of DR-COP versus R-EPOCH in patients with newly-diagnosed AIDS-related lymphoma. In the last 10 years, the treatment and survival of people with HIV-associated lymphoma has improved dramatically and the AMC strives to continually advance this field of research.

Jeffrey T. Schouten, MD, AAHIVS is a staff physician at the University of Washington AIDS Clinical Trials Unit and community representative to the AIDS Malignancy Consortium. Contact Schouten@u.washington.edu. Contact for Alexandra Levine, MD, 047 Protocol chair: alevine@coh.org.

For more details on study 047 see http://www.cancer.gov/clinicaltrials/AMC-047. Information about AMC research sites and all ongoing AMC trials is available at the AMC website: http://pub.emmes.com/study/amc/public/about/about.htm.

What's Love Got to Do With It?

The emotional side of serodiscordant relationships

by Keith R. Green

"I have a question for you, Keith," Roxanne interjected as we were concluding our interview on serodiscordant relationships (see *When Opposites Attract*, March/April issue). "Is it love? When someone who is HIV-negative decides to get involved or have sex with you after you disclose your HIV status to him or her, does that mean that they love you?"

The logical answer, I would think, would be yes. In an ideal situation, if someone who is HIV-negative chooses to become intimate with someone whom they know is HIV-positive, it *should* be safe to assume that the person's primary motivating factor is love or at least a fairly deep like for the other person, right? I mean, for what other reason would someone risk contracting a life-threatening, heavily stigmatized virus such as HIV?

Well, while working on that article, one of the underlying themes of more than a couple of the interviews that were conducted did, in fact, suggest another possible reason. And, while for the most part it was HIV-positive women who seemed to fall victim to this disturbing phenomenon, the HIV-positive gay men who were interviewed also alluded to having experienced it as well.

The "it" which I am referring to here is the "power dynamic" that seems to exist in many relationships where one person is HIV-negative and the other is HIV-positive—also known as a serodiscordant relationship. It can be best described as the pressure an HIV-positive person feels to conform to whatever structure the HIV-negative person desires for the relationship, simply because he or she wants to feel or be loved. Not surprisingly, the common risk factor among those who became trapped in such desperate situations appears to be a lack of self-esteem and self-worth that is the result of the ever-present stigma associated with HIV.

Roxanne, who spoke of how her sex life vastly improved after she was diagnosed with HIV and found no shame in discussing her rendezvous with multiple sex partners, admits that what she really wants more than anything is a solid, committed relationship with one man or woman.

"But people try to take advantage of you when they know you are HIV-positive," she claims. "I've even had men flat out ask me to pay them to be with them, telling me 'you know that nobody else is gonna be with you 'cause you got this virus.' The sad thing is that for a while I believed them and sometimes I went along with it. Until one day I thought, 'he must be crazy. I don't have to pay nobody to be with me.' "

Tony Stackhouse, a nationally recognized poet, author and vocalist, has never had anyone demand money of him, but confesses to frequently feeling expendable in his relationships because he is HIV-positive. "Dating brings out the best and worst in everybody," he claims. "HIV-positive brothers, myself included, have so many issues related to a lack of self-esteem and self-worth that we are, more often than not, impossible to date in any serious capacity. But, in all honesty, I think that HIV-negative men present just as much of a challenge. They come with a whole other set of issues."

Tony actually decided against having his most recent experience with dating an HIV-negative man printed in the original article because, at the time, they were facing serious complications in their relationship. They have since parted ways and, while he was still very skeptical about sharing the specifics of their breakup, Tony had no problem admitting that the most pressing problem they faced was his HIV status.

"For the most part, I'm out about my status," says Tony, who speaks publicly across the country regarding life as a Black gay man living with HIV. "But he made me feel like I should hide it. He was so uncomfortable with me being openly HIV-positive that he would never come to my shows. In the beginning, he didn't even tell a lot of his friends that we were dating because he didn't want them to think that he was HIV-positive as well. It was wild."

Tony now realizes the emotional toll that this relationship, like many of the others he had been in with HIV-negative men, took on him. "It was really tough at times," he says in retrospect. "But I wanted to be in a relationship so bad that I was willing to work through it. And it didn't help that he was smart, fine as hell, financially secure, and willing to be with me knowing that I was HIV-positive. I didn't really think that I could do any better and he didn't do much to convince me otherwise."

Aside from the emotional compromises, Tony also talked about the compromises that he made sexually in order to make his partner feel comfortable. "From the beginning, I was clear with him that while I can be versatile, I am mostly a top. He said that he was versatile as well but, when it came down to it, he was so uncomfortable with bottoming for someone who is HIV-positive—even with a condom—that we *never* did that. So not only did I hold back from mentioning my HIV status as much when I spoke or performed publicly, I also stopped performing in bed the way that I really liked so that he could be comfortable and, hopefully, see just how serious I was about being with him."

"Obviously," Tony says in a defeated tone, "it wasn't enough."

Tamara Wilson could also relate to the sacrifices that many HIV-positive people articulate that they make when dating someone who is HIV-negative. Her story, though, is probably unlike any other that

you've ever heard and yet it is probably no different.

At 29 years old, she was an office manager for a Jackson-Hewitt income tax agency during tax season and a receptionist at their corporate office through the rest of the year. She and her steady boyfriend of two years had just purchased a house together and all was well, or so she thought.

Tamara admits that she and her beau were a serious party couple who drank, used drugs and hung out just about every Thursday through Sunday. They never missed work, however, and made enough money to support their extravagant lifestyle and maintain a fairly happy relationship. Everything would change just a few months shy of Tamara's 30th birthday, though, when she was the unsuspecting victim of the first major tragedy of her life—rape.

She was immediately tested for HIV following the incident but when the suspect was caught and found to be HIV-negative, she put the possibility of being positive completely out of her mind. That is until she received a visit from a Department of Public Health worker who informed her that she had, in fact, tested positive for the virus that causes AIDS.

At that moment, the fabulous life that Tamara had come to know began to crumble. Not only did she learn that she was HIV-positive, but she also learned that her boyfriend's daily trips to the trunk of his car and the subsequent short drive around the neighborhood weren't the result of a secret drug addiction after all. He *was* taking drugs, but not the kind that she suspected. He had known that he was HIV-positive before they met and had kept it a secret from her up until that point.

But that's a different type of serodiscordant relationship altogether—another article in and of itself.

The point is that the depth of this series of traumatic experiences left Tamara heartbroken and clinically depressed. She stayed in the house for more than two months straight—taking no visitors or phone calls, eating very little, neglecting her personal hygiene and not reporting to her job. It wasn't until her family orchestrated a strategically planned intervention that she eventually broke out of her shell, but only enough to allow her to regain some semblance of a normal life. The damage that had been done to her self-esteem would prove not so easily reversible.

He was okay with her HIV status, as long as she didn't tell any of his fellow Muslim brothers and sisters.

Then in 2004, still extremely vulnerable and somewhat desperate for love after several failed relationships, Tamara met the man of her dreams—or so she thought. According to her, he was the textbook description of tall, dark, and handsome. A devout Muslim and single parent to 11 of his 17 children, Ahmed (as we will call him) embodied everything that Tamara had prayed for. More than anything she wanted a family and this one came ready made—big time. Throw in the fact that her newly found knight-in-shining-armor made reference to her as the queen of his throne and mesmerized her with the sex of her life, and Tamara was what many would call "hooked."

They dated seriously for several months and eventually moved in together. She even began to frequent the mosque with him. Though it didn't necessarily appeal to her, she studied and adopted the lifestyle of Islam in an effort to show Ahmed how sincere she was about being with him. He was okay with her HIV status, as long as she didn't tell any of his fellow Muslim brothers and sisters. Muslim people, she learned, view people who are infected with HIV as dirty (or at least the ones Ahmed fellowshipped with did).

In hindsight, Tamara believes that Ahmed was playing on her vulnerability from the very beginning. And, once he knew that he had her at his beck and call, she began to experience a side of Ahmed that she never would have imagined existed.

Tamara's self-esteem was so low and her desire for a family and love from a man so strong that she allowed Ahmed to convince her that she could be cured from HIV if she changed her diet and drank a daily concoction of herbs that he made for her. For almost a year she stopped visiting her doctor, stopped taking her antiretrovirals and became submissive and obedient to the life that Ahmed's Allah was mapping out for her. By this time he had officially become her husband.

Chastisement from Tamara's neighbor and friend, who was also HIV-positive, snatched her back to reality. She convinced Tamara to return to her routine doctor's visits so that she could at least know how she was doing physically. Tamara obliged, but the detour from taking care of herself and treating her HIV would cost her. Her T-cell count had dropped from over 800 to 202. Her viral load had gone from undetectable to somewhere in the tens of thousands. Not knowing how to leave, or even if she really wanted to, Tamara resorted to hiding her medication in the Weber grill on the back porch to keep Ahmed from knowing that she had disobeyed him.

Eventually, after much heartache and disappointment (and a couple of fights that placed both of them in the county jail), Tamara parted ways with Ahmed. Now she is struggling to regain control of both her physical and emotional well-being.

"I'm learning to love myself now," she tells me from her hospital bed in a suburb of Chicago. "I had to go through all of that to learn that nobody is going to really love me until I start loving myself."

Roxanne, Tony, and I could not agree with her more.

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
REYATAZ® (RAY-ah-taz)
(generic name = **atazanavir sulfate**) **Capsules**

℞ **ONLY**

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

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New Drugs at CROI: The Four Musketeers

New drugs, new targets, new hope

by Jeff Berry

To access Webcasts and Podcasts from many of the conference sessions, visit www.retroconference.org. For additional Webcasts of interviews with activists and researchers held during the conference, visit https://ifara.info/ and click on the video library, or go to http://video.google.com/videosearch?q=croi+2007&hl=en.

The most exciting news to come out of the 14th Retrovirus Conference held in Los Angeles during February related to new drugs currently in development, including two integrase inhibitors, an entry inhibitor, and a second-generation non-nucleoside. Dr. John Mellors of the University of Pittsburgh introduced the late breaker session on Tuesday evening, remarking, "I don't think it's an understatement to say that this session marks a milestone in the treatment of HIV in resistant patients."

Photos © Jeff Berry

Raltegravir

In the late breaker session on Tuesday, David Cooper, MD of the University of New South Wales in Sydney, Australia presented 16 and 24-week data from Phase 3 studies of Merck's integrase inhibitor raltegravir (formerly known as MK-0518). Integrase inhibitors belong to a new class of drugs that target HIV at a different point in the HIV lifecycle. BENCHMRK-1 & BENCHMRK-2 are two identical studies under investigation in different countries, with approximately 350 patients in each study. The randomized, double-blind, placebo-controlled studies looked at raltegravir 400 mg twice-daily in combination with optimized background therapy (OBT). Patients were generally heavily treatment-experienced, with resistance to at least one drug in each of three classes (NNRTI + NRTI + PI) upon entering the study. Participants had the following characteristics: an average age in the mid-forties, 150 T-cells, a viral load of 4.5 logs, and 10–11 years on therapy. Most had tried an average of 12 different HIV medications. The drug was generally well tolerated with a safety profile comparable to that of OBT plus placebo. Few adverse experiences led to discontinuation of the drug.

Approximately twice as many patients on raltegravir achieved undetectable viral loads compared to those on placebo (77% less than 400 copies/mL and 61% less than 50 copies/mL). In both studies, 61% of those resistant to all other drugs in their background therapy still achieved a viral load less than 400 copies/mL at 16 weeks, an impressive result. In a combined analysis of the two studies, when raltegravir was given with Prezista and/or Fuzeon, more than 90% of patients achieved a viral load less than 400 copies/mL. CD4 cell counts increased between 83–86 cells/mm^3 in both groups, more than 2–3 times those in the placebo group.

In a subgroup analysis looking at the percentage of patients with HIV RNA viral loads less than 400 copies/mL at week 16 by baseline viral load and CD4 cell count, 63% of patients with less than 50 T-cells, and 86% of those with more than 200 T-cells at baseline achieved less than 400 copies/ml. In this same analysis 88% of those with a baseline viral load of less than 100,000 copies/mL achieved undetectable viral levels vs. 55% on placebo; 64% of those with more than 100,000 copies/mL achieved less than 400 copies/mL compared to 19% of those on placebo.

(For more about raltegravir and other new drugs see One-on-One with Joseph J. Eron, MD on page 31).

Maraviroc

Also at Tuesday's late breaker session, Howard Mayer, MD of Pfizer presented 24-week data on their oral CCR5 antagonist maraviroc, which belongs to an entirely new class of drug that blocks HIV at the point of entry into the CD4 cell. MOTIVATE 1 & 2 are two identical Phase 2b/3 trials ongoing in different countries, with 601 and 475 patients respectively. Patients were randomized 2:1:1 to receive optimized background therapy (OBT) plus 150 mg maraviroc once or twice daily. To be eligible for the study participants had to have CCR5 (R5) tropic virus, a viral load of at least 5,000 copies/mL, be on a stable antiretroviral (ARV) regimen or no ARVs for at least four weeks, and have resistance to and/or a minimum of six months experience with at least one ARV from three classes (at least two for PIs).

In MOTIVATE-1, which is being conducted in the U.S. and Canada, at baseline the mean age across all groups (OBT plus placebo, once-daily or twice-daily maraviroc) was 46 years; the majority were Caucasian (at least 90%) and male (81-84%). The mean reduction in HIV-RNA viral load from baseline was 1.82 log for the maraviroc once-daily group and 1.95 logs in the twice-daily group, versus 1.03 logs in the placebo group; the mean increase from baseline CD4 at week 24 was 107 cells/mm^3 in the once-daily group and 111 cells/mm^3 in the twice-daily group, versus an increase of 52 cells/mm^3 in the placebo group.

In a combined analysis of the two studies, the most pronounced differences in viral load reduction between those on drug and those on placebo were seen in those with one to two active drugs in their OBT: for those with one active drug in their OBT, 43% reached a viral load less than 50 copies/mL in both the once-daily and twice-daily groups vs. 9% in the placebo group; for those with two active drugs in their OBT, 52% of those on maraviroc once-daily and 53% of the twice-daily group achieved a viral load less than 50 copies/mL vs. 19% for the placebo group.

There were no significant adverse events in either study. There was some concern, however, about the potential development of lymphomas and other malignancies, which occurred during the study of a second CCR5 antagonist, vicriviroc, though no definite cause-effect relationship has been shown. The study of a third CCR5 antagonist, aplaviroc, was terminated because of damage to the liver.

In summary, the authors concluded that maraviroc once-daily and twice-daily plus OBT "demonstrated significantly greater virologic suppression compared to placebo plus OBT in this treatment experienced patient population." They added that there were "no clinically relevant differences in the safety profile between maraviroc and placebo treatment groups." Also, "fewer patients receiving maraviroc experienced treatment failure compared to those receiving placebo; however more patients on maraviroc had a change in tropism result to D/M [dual/mixed-tropic virus] or X4 [CXCR4-tropic virus] at time of failure." However, it was also noted that in this category the mean CD4 increase of maraviroc patients "was greater than that seen in the total placebo group who failed therapy."

> "I don't think it's an understatement to say that this session marks a milestone in the treatment of HIV in resistant patients."

Elvitegravir

Andrew Zolopa, MD of the Stanford University School of Medicine presented 24-week data on the Phase 2b study of Gilead's integrase inhibitor elvitegravir, formerly known as GS-9137. Elvitegravir requires boosting with 100 mg Norvir (ritonavir) and is dosed once-daily. Studies are moving forward with the 75 mg dose. The study, initially designed as a non-inferiority study, looked at 278 highly treatment experienced patients with a viral load HIV RNA of at least 1,000 copies/mL and at least one protease mutation, with an optimized background therapy (OBT) containing two or more NRTIs but no NNRTIs, while nearly 20% were on Fuzeon (efuvirtide, T-20). There was a comparator boosted-PI group of which 49% were on Prezista (darunavir) and 27% taking Aptivus (tipranavir). Three doses of boosted elvitegravir were initially studied, 20, 50, and 125 mg. However, the 20 mg group was discontinued at week eight at the recommendation of the Data Safety Monitoring Board (DSMB) due to a high rate of failure, at which point patients were offered open-label elvitegravir 125 mg. The DSMB also recommended permitting the addition of Prezista or Aptivus to the elvitegravir arms due to lack of drug-drug interaction with elvitegravir. As a result of these changes, only 16 and 24-week data were given. At 16 weeks a viral load of less than 50 copies/mL was seen in 38% of

those on 50 mg elvitegravir and 40% of those on 125 mg elvitegravir, versus 30% in the PI group. By week 24 this was reduced to 32%, 36% and 27 % respectively. At 16 weeks, increases in mean CD4 cell counts were 52, 61 and 28 cells/mm^3 in those on 50 or 125 mg elvitegravir or a comparator PI, respectively. At 24 weeks increases in CD4 cell counts were similar in all groups. Phase 3 studies are now being planned with a 150 mg tablet which is bioequivalent to the 125 mg currently being studied.

In a related poster (627) by G. Jones, et. al., the authors identified two primary resistance patterns that cause reduced susceptibility to elvitegravir. This could possibly lead to cross resistance with Merck's integrase inhibitor raltegravir, but not to other antiretroviral drugs currently available or in development, including NRTIs, NNRTIs and PIs.

TMC-278

Anton Pozniak, MD of Chelsea and Westminster Hospital in London, UK gave a late breaker presentation on TMC-278, Tibotec's second generation non-nucleoside that is currently in a randomized, controlled Phase 2b dose-finding study in treatment-naïve patients. TMC-278 has a long half-life (45 hours) and has been shown to be highly active against wild-type and drug-resistant HIV *in vitro*. A total of 368 patients, 30% who were women, were randomized to receive a backbone of two nukes (Combivir or Truvada) plus Sustiva (efavirenz) 600 mg once-daily or TMC-278 25, 75 or 150 mg once-daily. All arms performed well in the study and there was no statistically significant difference in efficacy among any of the treatment arms. Of those on TMC-278, 77-81% achieved a viral load less than 50 copies/mL at 48 weeks. The mean change in viral load was approximately -2.6 logs in all four groups. Mean CD4 T-cell count increases were also similar across all four groups, between 125 and 145 cells/mm^3. The most common adverse events were nausea (TMC-278 35% vs. Sustiva 29%) and headache (18% vs. 16%). Nervous system disorders and psychiatric events were lower with TMC-278 (28% and 13% respectively) compared with Sustiva (48% and 16% respectively). Rash was less frequent for TMC-278 (8%) vs. Sustiva (19%), and total cholesterol/triglycerides were lower with TMC-278 than with Sustiva. No significant differences in serious adverse events were seen among the four groups. Development is moving forward with the 75 mg dose once daily.

> There were no significant adverse events in either study.

Special thanks to Ross Slotten, MD for his review of this article.

Photos © Jeff Berry

Conference Round-up

New lipo drug, rapid testing, and more news from CROI

by Enid Vázquez

To access Webcasts and Podcasts from many of the conference sessions, visit www.retroconference.org. For additional Webcasts of interviews with activists and researchers held during the conference, visit https://ifara.info/ and click on the video library, or go to http://video.google.com/videosearch?q=croi+2007&hl=en.

News from the 14th Annual Retrovirus Conference, held in Los Angeles in February.

New therapy for stomach fat

Dr. Steven Grinspoon of Massachusetts General Hospital reported good results with TH9507, a drug available only in clinical studies that is being used to reduce the increased stomach fat often seen after use of HIV drugs. The research team not only saw more than twice the fat reduction that they were hoping to see, but a significant decrease in blood lipid levels as well.

"Cardiovascular risk is ignored too much by the press and the media. Abdominal fat is itself a significant indicator of cardiovascular risk," Grinspoon said in a press conference.

After 24 weeks of once-daily subcutaneous injections, there was an average 15.2% decrease in visceral adipose tissue (VAT), compared to an increase of 5% for the placebo group (people taking fake medication). Results are from abdominal CT (CAT scan).

Visceral fat is deep. Sitting directly on the internal organs, it is more dangerous in regards to cardiovascular disease than subcutaneous fat, which is superficial, lying underneath the skin.

Waist size dropped by an average of three centimeters (slightly more than one inch), but the results of detailed questionnaires of the people in the study are not out yet, so it's not clear how much of a difference they are seeing in their appearance. (In an e-mail to *Positively Aware,* one study participant said his doctor told him that "unsafe sex" was a side effect of the drug, as people renew their social lives.) Swollen waistlines are not only dangerous, but deeply distressing, and have prevented many people from going on HIV therapy.

Grinspoon said there was an 18% change in triglycerides, which is "better than some lipid-lowering drugs even though this is not a lipid-lowering drug."

TH9507 is a growth hormone releasing factor analog. Growth hormone itself has long been used by people with HIV to control stomach fat. "We did *not* give growth hormone," Grinspoon explained. "We gave a precursor [beginning step] to growth hormone. It's a more natural, more gentle physiological way to promote the body's own growth hormone."

Headache and arthralgia (joint pain, but without swelling) were seen in more than 10% of both therapy and placebo groups. Grinspoon said the treatment is much more tolerable than growth hormone. There was no significant change in fasting or 2-hour glucose and insulin levels. This was important because increased blood sugar and insulin levels are seen with growth hormone.

Results from a "confirmatory" study are coming from Europe, Canada, and the U.S., Grinspoon said. (In Chicago, the study is being conducted at Northstar Healthcare.)

In an interview with Medscape.com, Dr. Andrew Carr, an HIV specialist from Australia who's conducted research on lipodystrophy, said, "I'll be very interested to see whether the second Phase 3 trial can show the same results. If it does, then this is obviously going to be one potential—and the first proven—strategy for visceral adiposity in this patient population."

"A similar change to growth hormone should be a good thing, but real effect on heart health would take a long time and a lot of money to see," Grinspoon said. "I urge you to help us raise the money and we will give you those results."

Rapid HIV testing and STIs in San Francisco

The San Francisco Department of Health tried something new in its efforts to contain the epidemic. Gay and bisexual men who tested positive with the use of a rapid HIV test were started on treatment for chlamydia and gonorrhea at the same time without waiting for those test results to come in. It's known that having one sexually transmitted infection (STI) increases the risk of becoming infected with HIV, and vice versa.

Sure enough, the department found that men newly diagnosed with HIV were two-and-a-half times as likely to also have chlamydia as men who tested HIV-negative, and more than twice as likely (2.2 fold) to have gonorrhea.

These children are underrepresented in HIV treatment, with only a small percent receiving therapy for the virus.

Sure enough, the department found that men newly diagnosed with HIV were two-and-a-half times as likely to also have chlamydia as men who tested HIV-negative, and more than twice as likely (2.2 fold) to have gonorrhea.

In terms of percent, 22.7% of the men testing positive (50 out of 220) had chlamydia vs. 8.9% of those testing negative (426 of 4,809). For gonorrhea, 27.3% of the positive men (60 of 220) had it compared to 12.3% (592 of 4,809). Results are from 2004–2006.

"The high prevalence of chlamydia and gonorrhea, regardless of HIV status, highlights the importance of screening for both infections at all exposed anatomic sites. …Presumptive same-day chlamydia and gonorrhea treatment among gay men with newly identified HIV infection should be studied to limit the further transmission of both STD and HIV," the department noted in its abstract.

In presenting the department's findings during an oral session, Katherine Scott said the department is moving towards 100% rapid testing.

Treating herpes and HIV

More news on STIs and HIV: a collaboration between the U.S. Centers for Disease Control and Prevention (CDC) and the Thai government found that herpes treatment in positive women helped reduce the amount of HIV shedding in the genital tract. Eileen Duime of the CDC noted that herpes doubles the risk of getting infected with HIV. Fifty of 67 women (75%) had HIV shedding at enrollment into the study, and herpes treatment with acyclovir led to a reduction in shedding for 34 of them (55%). Duime said the researchers hope that the results will help inform policies on acyclovir suppression.

Risk reduction: Don't get crazy

Dr. Ume L. Abbas of the University of Pittsburgh and colleagues used a "complex mathematical model" to estimate the effectiveness of PrEP on heterosexual HIV transmission in sub-Saharan Africa. (PrEP stands for pre-exposure prophylaxis—the use of HIV medications before exposure to prevent infection.) PrEP could be very helpful in slowing the epidemic, but she said that in another scenario, if people stop taking PrEP and continue their sexual risk behavior, it will not have a significant public health impact. Similar findings have been reported before, including studies in people. Medicines can serve as prevention, but so can risk reduction.

Not leaving children to die—the Baylor international model

Dr. Mark Kline reported on the Baylor College of Medicine International Pediatric AIDS Initiative (see also the March/April 2006 *Positively Aware*). Kline led the Houston institute, which was already providing pediatric HIV care, to open clinics around the world to serve other children.

Kline reported that as of the end of 2006, there were 2.3 million children around the world infected with HIV, with approximately 530,000 new infections last year alone. These children are underrepresented in HIV treatment, with only a small percent receiving therapy for the virus. In Botswana, where the first BIPAI clinic on the African continent opened, 57.7% of all deaths under the age of five are due to HIV/AIDS.

There are seven clinics in Africa (Botswana, Burkina Faso, Lesotho, Libya, Malawi, Swaziland, and Uganda), one in Romania, and one in China. Median CD4% is steadily increasing with the length of time the centers are in existence. Ninety-three percent of the children treated remain alive and on treatment, with only 10% needing to switch their therapy.

But Kline said it is not enough. "Pilot programs must be scaled up quickly to serve 800,000 children in urgent need of HIV care," he told his audience.

In addition, BIPAI often treats adult members of the children's family. "We care for families or arrange for care in clinics nearby. Across Africa children are being therapeutically abandoned as the adults are receiving care. We don't want to do that to their families," Kline said.

Another important goal of BIPAI is to train the country's own medical providers, including many recruited back after having left for better-paying positions elsewhere. BIPAI does not recruit people already working in public health. All in all, the initiative provides support for regional and national scale-up of pediatric and family HIV/AIDS care and treatment.

Author's note: Doctors and interns interested in joining the Pediatric AIDS Corps should visit www.bayloraids.org.

News Briefs

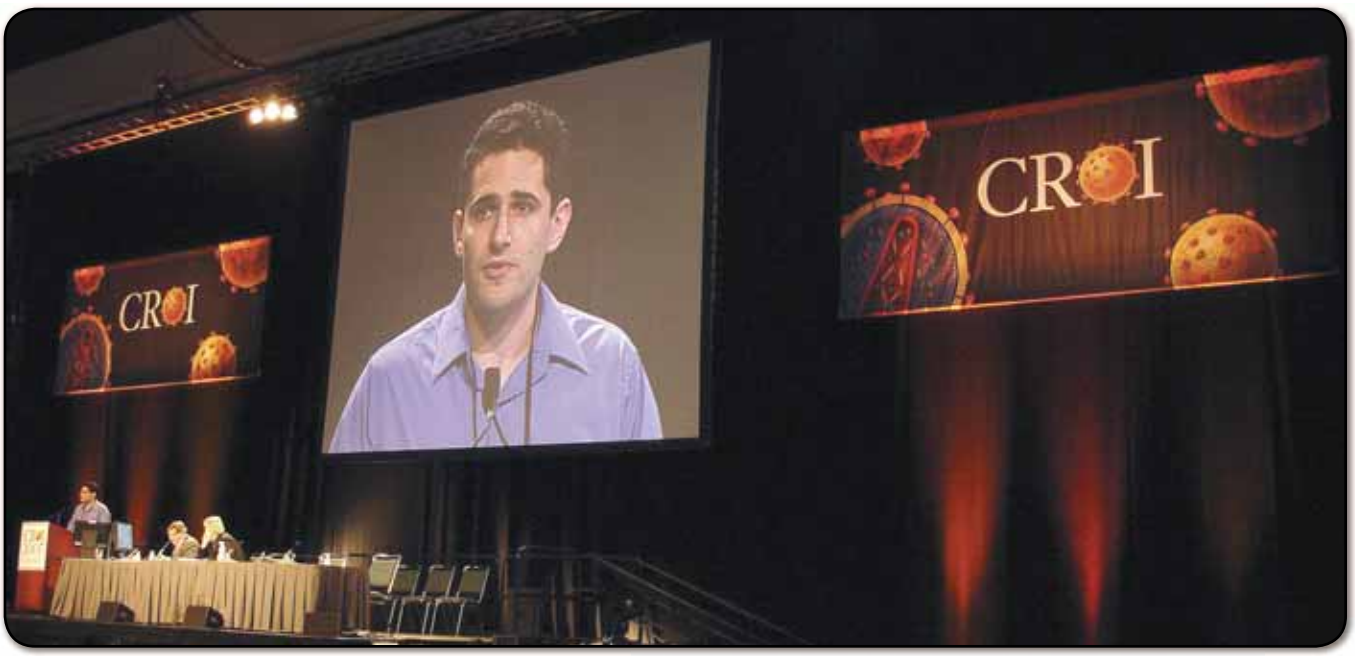
Hepatitis B drug Baraclude may cause HIV drug resistance; Women in HIV vaccine study wrongly told they are positive for the virus by outside medical providers. Visit www.tpan.com or see the upcoming July/August 2007 *Positively Aware.*

Photos © Jeff Berry

HIV Prevention Update

Some bad news, some good news

by Matt Sharp



Despite the fact that antiretroviral therapy has made a significant impact on the survival of people with HIV, the epidemic still rages on. Cases of HIV are being reported all over the world at a still alarming rate. In the U.S. African Americans are being disproportionately impacted and new infections in middle-aged and young gay men are increasing once again.

We are at a crucial moment in AIDS history where new prevention technologies are coinciding with the burden of new infections and they are gaining attention due to more and more research. At the International AIDS Conference in Toronto this past summer HIV prevention gained ground as the world was brought together to focus on the worldwide pandemic. Now, at CROI there appeared to be an even better focus on prevention possibilities, especially in the biomedical realm. It is now becoming more apparent that we may soon have a range of prevention possibilities as we currently have several treatment options.

At CROI there were dozens of important papers presented on the state of HIV prevention research. There are currently five prevention technologies in 14 ongoing clinical trials. To date, only three approaches have been proven through randomized clinical trials—male circumcision, antiretroviral prophylaxis to prevent vertical transmission, and contraception barriers for HIV prevention. But prevention strategies that made the biggest news at CROI include antiretroviral pre-exposure prophylaxis (or PrEP), male circumcision, vaccines, and microbicides (see vaccine update on page 28). Other methods for HIV prevention have less evidence, but the foundation has been laid for effective prevention strategies. In the next four years, results from these 14 studies will hopefully give us a shot in the arm for possibilities in stemming new HIV infections.

The unfortunate news for prevention at CROI was the CONRAD trial using a cellulose sulfate vaginal microbicide that was held in several developing countries and the U.S. At least two studies were closed when they discovered that women randomized to receive the microbicide were at an increased risk of HIV infection. It's not clear why this product did not prove effective in these studies, however, other work is being done in several other candidates, including different compounds and rectal microbicides. This disappointing trial closure is not a reason for giving up, as there are many other ongoing clinical trials and much preclinical work being done in different targets and with different products. As in all research, there are occasional pitfalls while there are also gains being made.

A controversial yet potentially big breakthrough in HIV prevention is the use of antiretroviral medications to prevent exposure

to HIV. Called PrEP (pre-exposure prophylaxis), one study is currently looking into whether Truvada or Viread is effective in preventing HIV transmission. There was no PrEP data presented at CROI except for one CDC survey that asked if gay men had ever used PrEP before. The concern is gay men will use PrEP thinking they are protected from HIV before the strategy has been proven. There are widespread rumors that there is a lot of "off-label" use of PrEP in the gay male community, but there are many issues about toxicity and resistance not to mention effectiveness using this strategy that still need to be answered. The survey reported that out of 400 HIV-negative gay men, 0.3% said they had used PrEP before. Almost 22% said they had heard of PrEP. The survey was given at Gay Pride events nationwide.

Male circumcision has become an important strategy to consider when talking about HIV prevention due to several studies that have shown it to be effective in up to 50–60% of cases. At CROI two major late breakers showed that circumcision may reduce genital ulcers and thereby reduce HIV transmission in a large randomized study in Uganda. However, another World Health Organization study of circumcision released after CROI showed the intervention was not effective for HIV-positive men with heterosexual HIV transmission. In this study the reason for the poor results were because men did not wait until their circumcision healed before they had sex with their partners, thereby most likely transmitting HIV to their female partners through open wounds. Male circumcision has many possible outcomes for reducing HIV transmission, but more work needs to be done to clarify how it can be most effective. It will continue to be a major prevention strategy.

Although it has always been said that HIV testing is not HIV prevention, the test site can be a great place to educate people about the risks of HIV transmission. New rapid testing technologies combined with HIV RNA screening and counseling may improve the opportunity of identifying those who may have recently acquired HIV and thus may be more infectious. Implementation of HIV testing at venues where high risk activity may occur is also a strategy that is proving effective. A study of rapid testing at New York City bathhouses showed a 5% seropositivity rate and that 40% of those were recently infected.

All of these new prevention strategies by themselves will most likely not be 100% effective; however, use of them in combination may improve the overall outcome. Combination prevention is a strategy that makes sense, just as highly active antiretroviral therapy (HAART) used combinations of medications and completely changed the lives of those living with HIV for the better.

To become more involved in HIV prevention advocacy, join the CHAMP (Community HIV/AIDS Mobilization Project) Action Network at www.champnetwork.org.

Photos © Jeff Berry

CROI Vaccine Update

Several HIV vaccine trials testing efficacy are underway

by Kevin Fisher

At the end of February, thousands of the world's leading HIV researchers and a few advocates met at the 14th Conference on Retroviruses and Opportunistic Infections (CROI). CROI, as it is known, is a scientific conference for HIV researchers in both the treatment and prevention areas.

Merlin Robb presented on the number of HIV vaccine efficacy trials planned or in the works. These trials are looking at the ability of a vaccine candidate to prevent infection or to slow or stop progression to AIDS. One trial, by the U.S. Military HIV Research Program, is testing a canary pox HIV vaccine with a protein boost in a large-scale clinical trial with 16,000 volunteers in Thailand. Another Merck-sponsored adenovirus vector candidate is being tested in 3,000 volunteers in the U.S. and Latin America. The adenovirus vaccine is based on a form of cold virus made harmless.

Two additional efficacy trials are also planned. A South African trial of the Merck candidate is scheduled to start this year, and a trial of the Vaccine Research Center (VRC) adenovirus vaccine is also planned. The canary pox vector vaccine is expected to have results by June 2009, with results from the Merck U.S. and Latin America trial by 2010. The South African trial of the Merck candidate is expected by June 2011, and the results of the VRC trial are expected about the same time.

Researchers believe that the Merck and VRC adenovirus vaccines have strong immunologic responses shown by higher levels of T-cells that recognize HIV. These T-cells could be stimulated to attack HIV infected cells and to slow HIV replication. Dan Barouch presented on a second generation of adenovirus vaccines that may provide even higher immune responses. The vaccines in efficacy trials will not generate the neutralizing antibodies thought by some necessary to prevent infection. Dennis Burton of Scripps presented a talk on why antibodies are so difficult to generate and suggested that an effective vaccine may need both antibody and T-cell responses.

Over the next few years we will begin to hear the results of clinical trials of these vaccine candidates. If they succeed, additional clinical trials may be necessary before they can be licensed. If these vaccines slow disease rather than prevent it, the vaccine field will also need to think about how they can be introduced and how they fit into the entire spectrum of HIV prevention technologies.

Kevin Fisher is the Senior Policy and Strategy Advisor for the AIDS Vaccine Advocacy Coalition (AVAC) in New York City. He can be reached at kevin@avac.org.

Astounding Choice in Breastfeeding: Infection or Death

Contradictions threaten the lives of infants in resource-limited countries

by Enid Vázquez

For centuries, all around the globe, women steadfastly breastfed their infants.

But in a world of poverty and disease, HIV-positive mothers face gut-wrenching choices with the concept that "breast is best."

The most difficult choice of all: breastfeed and risk HIV transmission to their infant, or withhold breastfeeding with its immune-building power and risk watching their child die of other diseases.

"If you choose breastfeeding, you would, of course, have HIV infections. No question about it," Hoosen Coovadia, MD, said during the 14th Annual Retrovirus Conference, held in Los Angeles in February. Breastfeeding could account for 300,000 new infant HIV infections per year, according to an estimate from the World Health Organization (WHO).

But a different figure, from UNICEF, estimates that 1.5 million babies would die each year if breastfeeding is not provided.

"So it's a balance of death vs. infection," said Coovadia in a plenary session. "And on the balance of probability, for poor women in the developing world, there is no other choice."

Although UNICEF takes into account all women regardless of HIV status, research continues to show the benefits of breastfeeding by HIV-positive women in the developing world.

Coovadia, of the University of KwaZulu-Natal in Durban, South Africa, outlined the current knowledge on breastfeeding in HIV-positive mothers in the developing world. His report included the latest information presented at this year's CROI. Among the disturbing reports: a study finding that the risk of infant death increased sharply within three months after breastfeeding was stopped in order to avoid HIV infection to those babies. (In countries like the United States, formula feeding is recommended for infants of HIV-positive mothers.) Coovadia conceded that the findings around breastfeeding are confusing.

Although HIV is present in breast milk, providing water to infants in areas where clean water is not available introduces parasites and other dangerous microbes into their tiny bodies.

Yet, with few—if any—good choices in the developing world, Coovadia, a longtime leader in caring for positive women and children, made the best possibilities shine through the grimness.

Pro and cons

Why would the cessation of breastfeeding lead to disease? Although HIV is present in breast milk, providing water to infants in areas where clean water is not available introduces parasites and other dangerous microbes into their tiny bodies. It is these dangers that can kill them, by causing diarrhea with its accompanying malnutrition, and pneumonia.

Years ago researchers reported that exclusive breastfeeding by HIV-positive mothers in developing countries was safer than mixed feeding. Mixed feeding is the introduction of water and food into the baby's diet along with the breast milk.

Tracey Creek and colleagues, on behalf of the U.S. Centers for Disease Control and Prevention (CDC), reported that the number one risk for death for infants admitted to an emergency room in Botswana was the lack of breastfeeding. The risk was higher than that of storing drinking water, overflowing latrines, stagnant water near the home, or unwashed hands of caregivers. All risks were adjusted for socioeconomic status, age, and mother's HIV status.

"But does breastfeeding protect infants of infected moms?" Coovadia asked. "The answer to that question was not planned for in these studies, but they tell a very compelling story. We have new evidence."

In that growing body of evidence is a report from the *Lancet* medical journal in 2003 which shows that breastfeeding is far and away the best protection against death before the age of five. Among the different protective factors, it accounts for 13% of all the deaths that could have been prevented by all the measures listed, higher even than the use of the HIV drug Viramune together with replacement feeding. ("This is not an either-or situation," Coovadia said.

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"We need both.") None of the other factors listed provided a double-digit protection.

What about the effects of withholding breastfeeding from HIV-positive infants? A report from the Mashi study from Botswana, reported in the *Journal of the American Medical Association* (JAMA) in 2006, found that early mortality was higher in formula-fed positive children than those who were breastfed and given AZT. At one month of age, death was 4.3% for formula-fed infants but 1.5% for the breastfed ones. At seven months, the difference was 9.3% vs. 4.9%. At 12 months, the figures came closer together: 10.9% vs. 9.5%.

"As the child grows older, the difference becomes less," Coovadia pointed out. "But here's the dilemma. At 18 months, more of the breastfed infants were infected, *but*, more formula-fed infants died."

Coovadia said an answer to this dilemma comes from a late breaker report at the conference from Louise Kuhn and Moses Sinkala and colleagues for the Zambia Exclusive Breastfeeding Study (ZEBS). Since various programs recommend that HIV-positive mothers cease breastfeeding sooner rather than later, ZEBS looked at the effect of cessation at four months of age. Not only was there no benefit in HIV-free survival as anticipated, but the risk of mortality was actually higher for both the HIV-positive and the HIV-negative infants who had stopped breastfeeding at four months.

The conference's abstract report from this study concluded that, "Our results caution against early cessation of breastfeeding for HIV-infected women living in low-resource settings. … Programs providing HIV diagnosis services should strongly encourage breastfeeding into the second year of life for infants found to be HIV-infected."

In another report, from Uganda, researchers found that early withholding of breast milk from HIV-negative infants caused greater risk of serious gastroenteritis, resulting in an increased rate of mortality within three months of cessation. The research was testing guidelines from the country's Ministry of Health that recommend abrupt weaning between three and six months of age to avoid HIV infection among infants of positive mothers.

In a press conference, Carolyne Onyango, MD, of the Makerere University-Johns Hopkins University Research Collaboration that conducted the study, said early HIV-negative results for the infants, provided to the mothers at two weeks and at four weeks after birth, led to discontinuation of breastfeeding. "There are statistics [supporting breastfeeding], but for that one mother whose baby gets HIV, that's a 100% result," she said. She also noted that the findings are preliminary, and the collaboration plans further analysis looking at other factors, such as the use of HIV medications and the mother's viral load. She and another doctor also brought up in passing simple things that might have helped the women and their infants achieve better health—a bar of soap to help keep hands clean, a container to keep water clean after it's been boiled.

Coovadia mentioned new findings from his research team, which are in the process of being published, that along with other reports show that exclusive breastfeeding is best for infants of positive mothers. "It simply means, for heaven's sake, don't give water or bits of food or whatever else," he reported. "Exclusive breastfeeding lowers the risk of transmission. That point is made time and again."

For one study of thousands of children in Zimbawe, exclusive breastfeeding up to six months had an HIV transmission rate of 1.3%. "It's as low as any antiretroviral," Coovadia pointed out. There were higher rates of 3% for children who were predominantly breastfed and 4.4% for those who were partially breastfed. "This is an absolute and convincing dose effect of exclusive breastfeeding and transmission rate," Coovadia told his audience. He discussed other studies which support exclusive breastfeeding in positive mothers. In one of them, adding a solid to the baby's diet led to a 10-times higher rate of transmission. Providing infant formula led to a 2-times higher transmission rate. "So a solid is very dangerous," he said.

"It simply means, for heaven's sake, don't give water or bits of food or whatever else," he reported.

Yet, he noted, women do not exclusively breastfeed, and further, doctors report that it's "impossible" to change that fact. "I told you that 99.9% of women don't exclusively breastfeed. So how do you change this? We did," Coovadia said. "The point is we *can* change behavior." The catch: it cost millions of rands (the South African monetary value) through a generous grant, and involved both counseling and home visits. Nevertheless, said Coovadia, the point of principle was made.

"For me and for my colleagues," said Coovadia, "and for many people like us who work in the developing world, we can't give up on women and breastfeeding. That to me is too easy, too glib an answer. Most of the efforts of my colleagues presented here are really trying to make breastfeeding safe for women where they are, how they live, and hopefully, within the next few years. [Use of infant] formula did not work going from the West to the developing world. We have to find our own solutions. We have to make exclusive breastfeeding socially acceptable."

Author's note: For a Webcast or Podcast of Coovadia's presentation, visit www.retroconference.org.

One-on-One with Joseph J. Eron, MD

by Jeff Berry

During the 14th Retrovirus Conference I had the opportunity to sit down with Dr. Joseph Eron, Associate Professor of Medicine at the University of North Carolina-Chapel Hill, and one of the investigators for BENCHMRK-2. Dr. Eron graciously took time out of his hectic conference schedule to talk in-depth with Positively Aware *about raltegravir as well as some of the other new drugs that will soon become available, and what it all means in terms of new options for both treatment naïve and experienced patients.*

Berry: Could you give us an overview and some of the highlights from BENCHMRK-1 and 2?

Eron: The overview and some of the big picture results are that in very highly treatment-experienced patients, Merck's integrase inhibitor raltegravir—as it's now called—added to other HIV drugs was significantly better than the background therapy of HIV drugs combined with placebo. These are 16-week results and, while it's a planned analysis, it's kind of an early analysis. Three-quarters of the people in both studies, however, got below 400 copies, compared with approximately 48% in the placebo arm. This is highly statistically significant. The other important thing to point out is how well tolerated raltegravir was compared to placebo. There is a very long list of potential adverse reactions, but there was a kind of similar response between placebo and raltegravir.

B: Wasn't there one AST (liver enzyme) that was elevated in one group?

E: Yes. I think it wasn't really consistent across the two studies. It was different in one study and kind of flipped around in the other study, so I think it was really generally stacking up as being very well tolerated. The other factor that we're learning, or we keep relearning, is that when the integrase inhibitor was combined with more active agents, we saw an even better effect. This was broken down very nicely for us in this study.

B: These were people who were new to darunavir [Prezista] or enfuvirtide [Fuzeon]?

E: Yes. We did a subset analysis that looked at patients who were receiving enfuvirtide for the first time, receiving darunavir for the first time, and also got the Merck integrase inhibitor. Again [it's] a subset analysis, so these are smaller numbers, but 98% of those people were less than 400 [copies/mL], which is really kind of remarkable. If you look at the numbers, it means just one person in that group of 44 people didn't get less than 400. And that's with a typical "missing equals failure" analysis where dropouts, or toxicity dropouts, would be included as failures, so I think it's pretty encouraging. And then if you look at the breakdown, if they were naïve to enfuvirtide and got it and didn't get darunavir but got the integrase, it was about 90% [below 400 copies/mL], and the same if you flipped it around. I think what it's telling us is that as clinicians, we need to keep our eye on the ball and make sure if we're changing therapies for our patients that we're actually combining active drugs. It's great to have an exciting new investigational agent that works by a new mechanism, but we need to pay attention and make sure the background is solid behind this drug.

I think that's why people like Dr. Mellors are saying that we are in a different era.

B: Dr. John Mellors talked about these new drugs, including maraviroc, as marking a "milestone" in the treatment of HIV in resistant patients. Do you feel that way?

E: I think that's the way that I think about it. If we got less than 400 copies just three or four years ago, even in treatment-naïve patients, we would be very pleased. I think that's why people like Dr. Mellors are saying that we are in a different era. What these data show is that if you combine this drug with other active agents you see

Photos © Jeff Berry

these very strong responses. And then you hear about maraviroc and etravirine [TMC-125] and TMC-278 [Tibotec's other NNRTI], and while we don't know for sure, one would anticipate that combining these drugs with raltegravir is going to get the same kind of good result.

B: So you're "cautiously optimistic"?

E: I'm a little bit cautious, yes. I think we need to see longer-term data. We saw some of the continuation out to 24 weeks, but the whole population hadn't made it there yet. The studies will extend to beyond 48 weeks as I understand it, so we'll get the long-term data that we want to see.

> Drugs that are easy to administer and are well-tolerated tend to move forward.

B: That was actually one of my questions, because you always hear "48 weeks—don't get too excited until you get that 48-week data," and a lot of this data is early. So do you have to keep that in mind?

E: You have to keep that in mind. We are a little bit unfortunate with the Phase 2 data because we are kind of in between meetings. At ICAAC we saw 24-week, Phase 2 data, and it's a very similar design, though multiple doses, and obviously if there were 24-week data at ICAAC there are now 48-week data for that earlier study available. There just is no venue to present it at because the deadline for this meeting was months ago. So, I'm agreeing with you, I think that what we'll see, maybe in Sydney in the summer, is some of the more extended data. I do think that if you look at the POWER studies, for example, or even some of the older TORO studies, you'll see that for the most part, if people got below 400 [copies] or 50 in particular, at 24 weeks, you tended to see similar percentages. In fact, that was also published in the RESIST studies, so we can actually look at three now published studies, TORO, RESIST and POWER 1, where we kind of see that the proportion that is below 50 or 400 at 24 weeks is similar to what was then seen at 48. But I'm a cautious person—I don't want to extrapolate too far. But you're right, we want to see the durability of this drug—actually, all the new drugs that were presented.

B: Can you think of any other drug that demonstrated that kind of reduction in viral load in just two to four weeks?

E: Well, the reduction in viral load that was seen with raltegravir and certainly in the treatment of these patients was remarkable. No, I can't think of another single drug like that. There is published data on etravarine from years ago but it's hard to make cross study comparisons. I think that drop is really kind of remarkable. And again, it was a little easier to see in the Phase II naïve study; it wasn't really highlighted in yesterday's presentation, so I really don't know how the rate of drop compares. We do know that by two weeks, 60% of the patients are less than 400. I would say that's remarkable.

B: Pretty remarkable, especially in that there are really no interactions or side effects so far.

E: Right. The fact that the drug is glucoronidated is an advantage and it avoids the potential drug interactions with protease inhibitors, NNRTIs, anti-depressants, and statins. Also, it's not going to be boosted by ritonavir. The flip side, however, is that it's a twice-a-day drug. But I think the fact that it is glucoronidated will make it easier to combine with other drugs and we'll have to worry somewhat less about PK interactions.

B: So, what do you feel is the significance of the fact that it was a highly treatment- experienced group in terms of how the drug will be used in the general population?

E: I can only speak for myself as a clinician. I think that initially we will use this drug in the treatment-experienced population. My experience has been that drugs that are well-tolerated tend to then move forward in the treatment cascade. Drugs that are hard to administer—multiple pills, side-effects, etc., tend to stay in the later salvage. Drugs that are easy to administer and are well-tolerated tend to move forward. So, I can't predict the future but I think the fact that it is so well tolerated suggests that people might start experimenting with it. But again the data we have here is in a specific population.

B: What about those who have used both darunavir and enfuvirtide? Should they be adding raltegravir to their regimen, or should they be waiting for another active agent?

E: Yeah, I think the most difficult decision in clinical practice now is when to switch therapy in people who are treatment experienced. And I feel very strongly that it is a balance between clinical urgency and making sure you combine your new drug with other adequate drugs. My own opinion is that if someone is clinically stable, then it's wiser to wait for stronger partner agents. And you could ask, "Do I have a CD4 cell count threshold that I would say, definitely switch?" I don't think you can be that precise. Though I think if someone's got a new opportunistic infection and their CD4 cell count is falling, then I think you're forced to make tougher decisions. I think if someone has a good CD4 cell count, then it only makes sense to wait until you have other new agents in hand. I think that is sensible and the data from the BENCHMRK trials would support that—that it's better to have other active drugs in the regimen for sure.

My own feeling is that you're probably better off with more than two active drugs.

B: I'm sure you've probably heard from some providers that you need more than two active drugs, that you should have three if you're failing therapy.

E: Well, I think that the BENCHMRK studies suggest pretty darn good activity with two active drugs, when it was enfuvirtide plus the integrase or darunavir plus the integrase. On the other hand, there are other agents in the background here: they're getting nucleoside anologs. I think Andy Zolopa asked the question, "What was the average number of drugs in the background?" That's a question we should ask Merck because I'm not sure those data were presented. My own feeling is that you're probably better off with more than two active drugs. So I'd be more in the camp looking toward three active drugs, if you have that option. Then the T-20 [Fuzeon] sort of thing comes into play and patients have preferences about T-20. But, again 98% less than 400 with three active drugs makes it tough to argue. It will be great to see the durability in that population. I think if you have them and it's convenient and it's safe for the patient, then one should strongly consider using three active drugs. Because that's what we say for naïve patients, right? We wouldn't compromise in naïve patients. So, if you have that opportunity for treatment-experienced patients, then that would be one that I would take.

B: What about raltegravir resistance mutations and cross resistance to other agents?

E: What we know is that in this study, so far, there were 71 biologic failures and they were able to genotype 41—I think they just haven't gotten to all 71 yet and that was part of the presentation. Of those 41, nine did not have integrase mutations. We don't know if those people picked up a T-20 mutation or a darunavir mutation, we just don't have the information on those nine. 31 developed integrase mutations and they tend to be on one of two pathways. So, I think what could have been stated more clearly in the presentation is that it's not one mutation or another; there are typically groups of mutations. There is a 155 pathway and a 148 pathway. Typically what was seen were multiple mutations, suggesting a higher barrier to resistance. There was a presentation by another Merck scientist, John Wai. It was just *in vitro* work but, in that presentation, he suggested that if you have multiple integrase inhibitor mutations, there is likely to be cross-resistance amongst the two integrase inhibitors that are currently in clinical development. But I'm not a resistance maven, so I'm not completely sure.

B: Any serious adverse events? What should someone taking raltegravir look for or expect?

E: Well, I've treated 14 people now and it's kind of trite to say it's generally well tolerated, but I think it is very well tolerated. I can't point to a symptom or a problem either looking at the study or looking at the patients I've had the opportunity to care for to be able to say, "Oh, you should expect this."

B: So you haven't had any problems with adherence?

E: My experiences with most of the people who have gotten to this super-highly resistant state are usually people who actually listen to their doctor. They're people who took AZT and then 3TC [Epivir] and then added indinavir [Crixivan]. So my personal experience—outside of the study—is that most of my patients that have extensive triple-pass resistance are actually pretty adherent. My patients who are not very adherent tend to have less resistance; they tend to have NNRTI and 3TC resistance. So, in general, in any of the salvage studies that I've worked on, I haven't had a big issue with adherence. If you look at the TORO studies, and obviously T-20 has a huge barrier to resistance, most of the people in that study who failed therapy had resistance mutations, meaning they were taking the drug. I think that people in highly treatment-experienced settings take the medications. We would have to ask Merck how much adherence data they collected in this study. I don't remember. It would be good to know, but my sense is that adherence is quite good because tolerability is good. Almost all regimens that we have for these deeper salvage patients are twice daily. If you're going to incorporate darunavir, tipranavir or enfuvirtide for that matter, all those are twice-daily regimens. We don't really have a once-daily salvage regimen. Maybe that will come but we don't have it yet.

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THE K-11 UNIT

TEACHING—AND LEARNING—BEHIND BARS

BY JEFF BERRY

Left: Members of the Center for Health Justice staff (not pictured—Mary Sylla).

Below: Morris Jackson of the Center for Health Justice

In March of this year while in Los Angeles for the 14th Annual Retrovirus conference, I and several other members of the AIDS Treatment Activists Coalition (ATAC) were invited to give a talk on AIDS activism to inmates at the Los Angeles County Jail. I was a little apprehensive at first, as I'd never done anything like it before, but lately I've been feeling the need to go outside of my comfort zone, and so I accepted the invitation.

As we drove through the streets of downtown Los Angeles, hopped on the 110 for a few miles, and then rode through a dilapidated Chinatown, I started to second-guess my decision. Apprehension grew into a palpable fear as the twin towers of the County Jail loomed ever closer. The L.A. County Jail is the largest county jail system in the U.S., with close to 20,000 inmates at any given time, of whom 300 are known to be HIV-positive. Morris Jackson, Treatment Education and Prevention Specialist for the Center for Health Justice, was driving. During our ride we talked about some of the work the organization does at the jail, including transitional planning, referrals, counseling and testing, educational trainings, and condom distribution. I had no idea what to expect when we arrived at the jail, so I continued to pry Morris with questions as he drove, admitting that I was just a little nervous. He was finally able to soothe my nerves somewhat by informing me that he had never, in the year that he worked there, had a problem with any of the inmates.

As we entered the facility, the bars clanged shut behind us and the guard took our names and checked them against a list of approved visitors for the day. He held onto our ID and in return we were given a day pass that we clipped onto our shirts. We were told that if we lost the pass, the entire jail would go on lockdown and we would not be able to leave. Needless to say I checked more than once over the next few hours to ensure that my badge didn't come off.

We headed down several long hallways and rode the service elevator up to the K-11 Unit. This is where inmates who identify as gay, bisexual or transgender can voluntarily choose to live in a segregated unit. It allows them to live with others who they identify and share similar circumstances with and, most importantly, it keeps them out of the general population. But it's certainly no cakewalk. We stepped up into the observational booth and our arrival was announced over the microphone, inviting the inmates to join us for the presentation. I looked through the plexiglass out over three separate rooms, each one with rows upon rows of bunk beds, where dozens of men lived in each large room with a television and an adjoining shower area. No privacy here whatsoever. Many of these guys are in here on drug-related charges, and awaiting trial or transfer to another facility. Around 30% of those in the K-11 unit are infected with HIV—many do not find out they are HIV-positive until they end up in jail and choose to get tested.

Inmates were told that if they were talking or disruptive during the meeting, they would be sent back to the unit. Those who wanted to attend then lined up, and the thick steel door unlocked and swung open. They marched by, single-file, and we nodded and said hello, and many greeted us back. They proceeded to the room where the meeting was being held and lined up against the wall in the hallway near the door. As we walked by the inmates and entered the room before them, it suddenly struck me how I was completely out of my element and that I had entered another realm of reality—a reality that is a way of life for millions of people in this country.

Morris had told me earlier how incredibly ingenious some of these men and women are, crushing up blue pills to make eye-shadow, or carving tweezers out of a toothbrush. "Now if they could just take some of that energy and ingenuity and start to use it in a more constructive manner, they would be able to do something with their lives," he said with a glimmer in his eye, and I could see he really meant it. It was obvious to me that he and the other people who he works with really care about the inmates and that they definitely have a passion for this work. "I'm really lucky in the sense that I have a job that I look forward to going to every day. I work with

some incredible people, and I feel as though I'm able to make a difference in some of these guys' lives."

I was introduced to the group of about 50–60 men by Cathy Olufs, Education Director for the Center for Health Justice, who wrote the activist section for this year's *Positively Aware* Annual HIV Drug Guide, and who along with Morris is also a member of ATAC. "Now, you all know that magazine *Positively Aware* that we bring in here for you guys?" Many of them uttered in agreement and nodded their heads. "Well, this is the editor of the magazine." At that moment at least a dozen of them, as if on cue, held up the magazine. It was a moment that I will never forget. In that instant, I felt as though I was exactly where I needed to be and doing what I was supposed to be doing. The apprehension that I had experienced earlier suddenly dissipated.

Morris told the group that once they are sent to jail, people on the outside tend to forget about them, or don't even think about them at all. When I stood up to talk, I began with, "You know what? I *do* think about you guys. I think about you every single day. I get letters from you all the time, and I read every one of them. I don't have enough time to answer you personally, but if you request it, I'll make sure we add you to the mailing list, or send you information." I talked a bit about my own personal journey, and about the choices we make in life. I told them that no matter what circumstances we may find ourselves in, that we always are presented with a choice. As I spoke, it quickly dawned on me that had the circumstances in my life perhaps been a little different, or I'd chosen a different path, I could just as easily be sitting there alongside them listening to someone else give a talk about AIDS activism.

Nita Costello of Houston and Orlando Roman of New York City, fellow activist members from ATAC, engaged the group as well, making them laugh, sharing their own personal stories, and talking about how they came to be involved in AIDS activism. The inmates listened intently and seemed eager to learn as much as they could about HIV prevention, treatment, and advocacy. Their informed questions about drug interactions, adherence, HIV transmission, and resistance shattered many of the personal beliefs and stereotypes that up until then I had held about incarcerated individuals. You know—lazy, undeserving, uneducated. These guys were anything but those things.

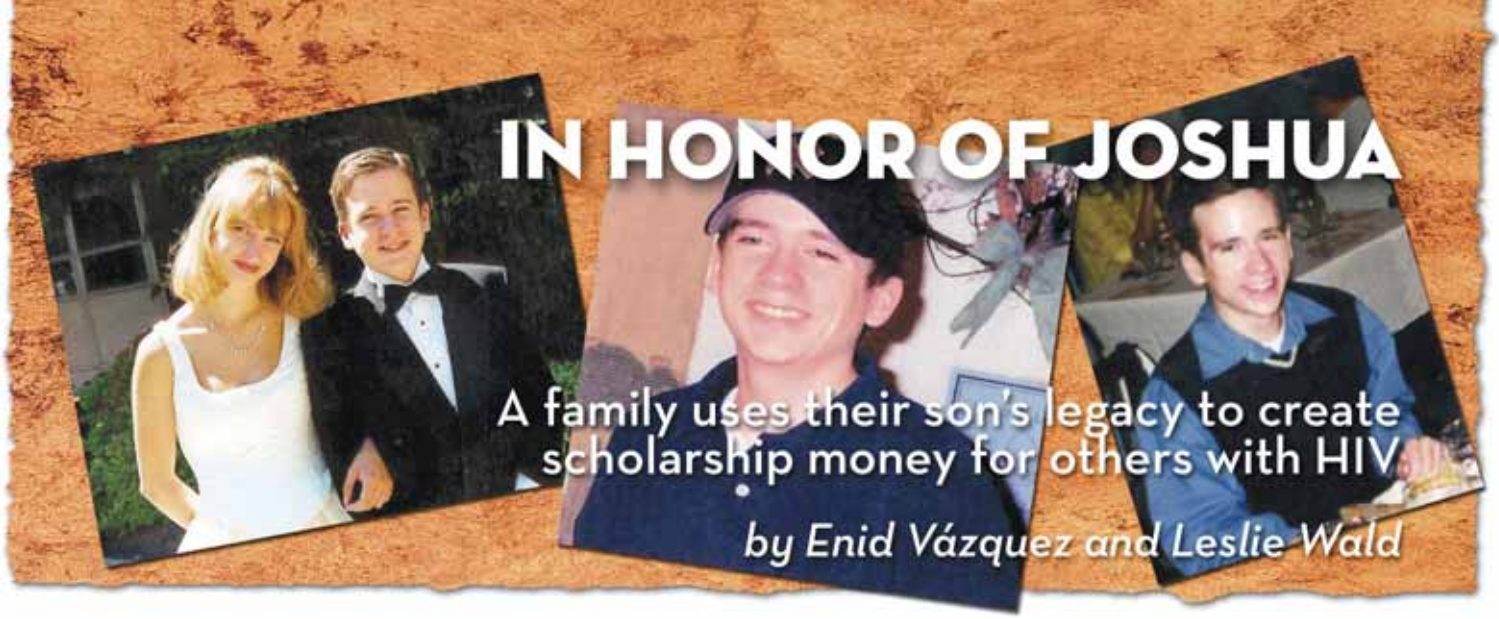
Our time was up much too quickly, and the inmates were told they had to leave and go back to the cell. Many of them came up to shake our hands and thank us personally. They seemed genuinely appreciative that we had given of our time and come to talk with them. It seemed so little to give, and I received so much in return.

Prison prevention

Today the debate on whether to allow condoms in prisons rages on. In 2006, Governor Arnold Schwarzenegger of California vetoed a bill that would have allowed condom distribution in state prisons. (However, a new bill is being introduced, AB1334, and is supported by a number of prison rights groups.) A recent Illinois House bill allowing condom distribution in state prisons was voted down six to five. But to me, the question of whether or not we should allow access to condoms in prisons seems moot. "Lock them up and throw away the key" is no longer an option in the age of AIDS. We have a moral and ethical responsibility to educate and empower *all* members of our society, regardless of who or where they are, and to provide them with the tools necessary to make safer and smarter choices—so they can protect not only themselves, but their partners and families as well. And until we offer comprehensive and non-judgmental prevention and education programs to all populations affected by the epidemic, we will never be able to stem the increasing rates of infection that continue to devastate our communities. It is as though we are handing down a sure death sentence. And their blood is on our hands.—Jeff Berry

About Center for Health Justice

With their newly-coined motto "Prisoner Health is Public Health," Center for Health Justice (CHJ) is a tiny agency doing big things around issues of incarceration and HIV/AIDS in California and beyond. CHJ was founded in 2000 under the name of CorrectHELP (The Corrections HIV Education and Law Project) by a coalition of AIDS activists, civil rights attorneys, and formerly incarcerated individuals who were concerned about the numerous unmet health needs of HIV-positive prisoners in California. Since its infancy, the agency's staff and supporters have worked tirelessly to achieve their mission—*to reduce the spread of HIV in prisons and jails, advocate for HIV-positive inmates, and reduce the recidivism rate for individuals affected or infected by HIV.* In early 2006, the Board of Directors voted to change the agency name from CorrectHELP to Center for Health Justice in an effort to better reflect their current work in the jails and prisons in California, which in addition to HIV prevention and treatment education services (including condom distribution in Los Angeles and San Francisco County Jails), now also includes educational programs on hepatitis C and STDs, women-specific empowerment programs, and a new public policy department focusing on broader issues relating to HIV in correctional settings. CHJ staff members are reflective of the communities they serve: nearly half are persons living with HIV/AIDS and several have previous incarceration experience. Under the leadership of a bright new executive director, Vincent Jones, a former staffer for U.S. Senator Barbara Boxer, Center for Health Justice is poised to move HIV and incarceration issues in the U.S. to the forefront in the coming years. CHJ operates an inmate hotline that accepts collect calls (323-822-3838) and is accessible to incarcerated persons around the country. For more information on Center for Health Justice or their programs, please visit their website at www.healthjustice.net or call (323) 822-3830.



IN HONOR OF JOSHUA

A family uses their son's legacy to create scholarship money for others with HIV

by Enid Vázquez and Leslie Wald

"Our son Josh died of AIDS five years ago," Mary Gomes wrote to TPAN last year. "In order to keep Josh's legacy alive we established a college scholarship for persons with AIDS. It is our goal to 'lay a path for hope' for young adults like Josh—those with HIV/AIDS—by providing academic scholarships to universities of their choice."

At the time of his death, Josh Gomes was 21 and working toward a double degree at the University of Denver for pre-medicine and pre-law. A hemophiliac, he contracted HIV at the age of two through a blood transfusion. Still, he always maintained a positive outlook on life. The opening lines of his scholarship website state that "Josh was a man with a plan. He had drive. He had passion. He had hope for the future." It is also said of Gomes, who was his high school valedictorian, that "learning was one of his core values: to stop learning was to truly die." But in looking for his own scholarship to college, he found that even many scholarships created in tribute to children with hemophilia who died from AIDS often went to those who weren't HIV-positive, and, "He believed that action spoke loudly: You may die, so we won't invest." Thus, the $1,000 scholarships given by his fund are attached with the message, "You are worth investing in."

Nineteen-year-old Brett Tucker, who was infected at age 16, agrees that some people have the opinion "you're not worth investing in," but says, "I think everyone is worth investing in, if given the right opportunities." Tucker said the $1,000 scholarship was very helpful, paying for all of his books at Johnson Smith University in Charlotte, North Carolina, where he is in his first year.

Does Tucker believe he has as much to offer as other students? "Yes, probably more so. My perception of time and value is altered."

Tucker took on a double major of English and psychology, and hopes to eventually earn a Ph.D. He also hopes that more people donate money to the scholarship fund so that more students can be awarded.

Mary Gomes said, "Here are people who just a few years ago had no hope of living and now they are reaching for and obtaining their goals and dreams. When one of the recipients recently called to tell me that he had been accepted at Oxford in England, I cried! He thanked my family for changing his life. I am really at a loss for words to describe the emotions that we have. It's almost like having an extended family that we are now cheering for and they are winning."

Her husband Steven Gomes added, "Our motto is 'laying a path of hope,' but this is so much more than hope. It is transformation. People's lives are changed by receiving this scholarship and living into their dream."

There's the young single mom with two kids (both HIV-negative) who works in a woman's clinic as a nurse's aide, helping other women also living with AIDS. "She needed to provide more for her children and she wanted to do more to help the women she was working with, so she dreamed of going to nursing school," Steven Gomes said. "Her clinic doctors recommended her, both for the extraordinary care she was providing to the other mothers, who were struggling with their health, but also with how to live their lives in the face of the threat of losing it all.

"This year, with Josh's scholarship, she began full-time classes in nursing school. She still works all day in the clinic and takes her classes at night. She is fulfilling her dream. Right now, she is incredibly busy with work, school, and being a mom. Her life is filled to the brim. We hear from her each week, about her excitement at accomplishing her goals and her happiness with two healthy children," he said.

The scholarships are based on merit and need. They are given to young adults with HIV/AIDS who share Josh Gomes' love of learning and community service. The application for the scholarship includes some brief questions along with an essay about the applicant's hopes, plans, and goals for the future.

The fund also accepts donations, in hopes of giving out more scholarships per year, and they will award as many as they take in funds for. The deadline for 2007–2008 applications is July 16th, 2007.

To donate, to apply

Mary Gomes says, "Since word has gotten out about our scholarship, we are being bombarded with applications from across the nation. Our only source of funding has been what our share of what our AIDS Walk team raises each year, and that isn't a whole lot. Since our start up five years ago, we have managed to give out 22 scholarships. We take absolutely no funds for administration costs and are a 501(c)3 [non-profit] organization."

For more information about Josh Gomes, to apply for this scholarship, or to donate to the Joshua Gomes Memorial AIDS Scholarship Fund, visit www.joshuagomes.org.

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Demystifying MRSA

Drug-resistant bacteria threatens HIV community

by Rupali Jain, Pharm.D.

By now you have probably heard of something called "MRSA infections" or "staph infections" from the news, or a friend. There have been outbreaks of skin infections caused by bacteria called MRSA in certain communities such as athletes, men who have sex with men, and HIV-positive individuals. MRSA can cause a wide variety of infections ranging from mild skin infections to serious infections such as pneumonia or sepsis. Patients with HIV are especially at risk due to their weakened immune systems.

Before we get into too many details, let's go over some basics.

What is MRSA?

MRSA stands for "methicillin-resistant *Staphylococcus aureus*." *Staphylococcus aureus* (also known as "staph") is a bacteria commonly carried on the skin or in the nose of healthy people. *Staphylococcus aureus* is carried in the nose by 10 to 40% of people in the community and the hospital environment.[1,2] When it is carried on the skin, it is not considered an infection because it is part of what is normally found on the skin and is not causing any symptoms.

MRSA is a type of staph bacteria that is resistant to a class of antibiotics called beta-lactams. Beta-lactam antibiotics include methicillin, penicillin, amoxicillin, etc. A smaller number of people carry MRSA in their nose and skin (approximately 1%) than those carrying *Staphylococcus aureus*.[1]

The history of MRSA

Staphylococcus aureus resistance was first described shortly after the introduction of penicillin in the 1940s. MRSA was reported one year after the introduction of the antibiotic methicillin in 1961. Today MRSA is a common hospital-acquired infection and it accounts for more than 50% of infections in the intensive care units (ICU).[3]

Up until several years ago, it was mainly considered an infection related to being hospitalized. The first cases of MRSA in the community were reported in the 1980s, but these occurred in patients who had contact with healthcare services. During the past decade, MRSA infections were occurring in healthy patients without a recent hospitalization.[3]

What is the difference between hospital-acquired MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA)?

There are several main differences between hospital-acquired MRSA and community- acquired MRSA:

1. CA-MRSA is less frequently associated with hospitalization whereas HA-MRSA is more frequently associated with a hospital stay.
2. CA-MRSA has less drug resistance, so more classes of antibiotics can be used against it as compared to HA-MRSA.

> Most commonly CA-MRSA causes skin infections that may look like a pimple or boil.

3. CA-MRSA contains a toxin that can cause tissue death and destroys white blood cells, and HA-MRSA does not usually have this.

A special test looking at the genetics of the bacteria can be done to distinguish between HA-MRSA and CA-MRSA, but this is not done commonly so it is based on clinical findings and the definition provided below.[4]

The definition of CA-MRSA is the following: [1]

1. Diagnosis of MRSA was made at the clinic or within the first 48 hours of admission to a hospital
2. No previous infection with MRSA
3. No previous history within the last year of being hospitalized, in a nursing home, or hospice, or receiving dialysis or surgery
4. No permanent medical devices that pass through the skin into the body (such as catheters) present

This definition is important for the doctors and nurses taking care of you so they can treat you appropriately.

How do I know if I am infected?

Well, before we go into detail about infections with MRSA, it is important to distinguish between colonization and infection.

Colonization (or being a carrier) with MRSA or staph bacteria does not mean you are infected. Bacteria normally live on our skin without causing any symptoms. Your skin itself serves as a blockade, not allowing for bacteria to enter your body. If the skin is cut or broken, the bacteria are given the opportunity to infect and it *may* cause an infection. It is important to remember that just because you are colonized with MRSA doesn't always mean you are at risk for infection. [5] People can be colonized in the nose (most commonly), the throat, the armpits, and the genital area. In 2001 and 2002 in the United States, it was estimated that 32% of non-hospitalized individuals were colonized with Staph bacteria and 0.8% were colonized with MRSA. [5]

There are certain groups of people that are at higher risk for being colonized or carriers of MRSA. These include HIV-infected individuals, injection drug users, patients with abscesses, and those recently hospitalized. [6]

Who is at risk for CA-MRSA infections?

There are several groups that have been identified that have a higher risk for CA-MRSA infections, and outbreaks (or clusters) of CA-MRSA infections have occurred among many of them. From these outbreaks, we can learn who is at risk for infection and target these people with prevention education.

Alaska Natives[4]: There have been outbreaks of CA-MRSA skin infections associated with prior antibiotic use.

Native Americans[4]: At an Indian Health Service facility in the Midwest, the number of MRSA infections increased over an eight-year period. Low socioeconomic class, crowded living conditions, and limited access to healthcare contributed to the high rate of skin infections.

Pacific Islanders[4]: A disproportionate percentage of patients infected with CA-MRSA at four healthcare centers in Hawaii were Pacific Islanders.

Prisoners[4]: In Georgia, California, and Texas, an increase of infections due to CA-MRSA among prisoners was associated with poor hygiene, limited access to medical care, and inadequate wound care supplies and staff. At many prison facilities, the inmates took care of their own wounds and boils as well as shared personal items.

Athletes[4]: Outbreaks of infection among wrestling, football, and fencing players have been reported. Most commonly the spread of the MRSA infection was caused by abrasions and cuts associated with the sport and the equipment and the physical contact. An outbreak of CA-MRSA infection even occurred in a professional football team!

Military personnel[4]: There have been several reports of CA-MRSA skin infections among military recruits and soldiers.

Children[7,8]: Some studies have indicated that children with CA-MRSA infections are increasing. Attending day-care may be a risk factor for some of these patients.

Men who have sex with men[9]: In Los Angeles, CA-MRSA skin infections in HIV-positive men who have sex with men were associated with high-risk sex and drug-using behavior and with environmental exposures. Immune status was not a risk factor but other studies indicate that the immune system may increase risk for infection.

HIV-positive individuals[1,10]: Outbreaks of CA-MRSA infections have been described in men who have sex with men (the majority of whom were HIV-infected) around the country in Los Angeles, San Francisco, San Diego, and New York. From the San Diego outbreak, researchers found that there were certain factors that increased risk for CA-MRSA infections, such as patients with HIV who acquired the infection via men who have sex with men or injection drug use. Also, patients with CD4 counts less than 50, higher viral loads, and absence of Bactrim therapy for prevention of PCP pneumonia were risk factors for CA-MRSA infections. Patients with HIV (or others with weakened immune systems) may be at risk for more severe illness if they get infected with MRSA.

Injection drug users: See above.

Many of the outbreaks listed above are associated with the spread of CA-MRSA infections via close skin to skin contact, open-

Case study

Ferdi is a 47-year-old male who is routinely seen at the HIV clinic. He was recently diagnosed with HIV and was started on antiretrovirals six months ago. He has no other significant medical problems. He lives in a group home for drug rehabilitation and was responding well to HIV treatment. He calls the nurse on Friday afternoon stating that he has a "small, red pimple" on his thigh and it may be a spider bite. He does not report any other symptoms and does not have any skin disorders. The nurse is concerned and tells him to go to the emergency room to have it evaluated. He ignores her advice and by Sunday, the pimple had grown and had become more painful. Ferdi goes to the emergency room. The emergency room doctors evaluate the pus-filled "pimple." They also notice the skin around the pimple to be warm and red. Ferdi is diagnosed with a boil and a skin infection called cellulitis.

What is the next step in the treatment?

The doctors drain the boil and send the fluid to the microbiology lab to find out what bacteria is causing this infection. Also, the microbiology lab will test different antibiotics to see which one will be effective for treatment.

The doctors then place a bandage over the wound. The preliminary results indicate the bacteria to be *Staphylococcus aureus*. The doctor also decides to give Ferdi some antibiotics for 10 days.

Why was Ferdi at risk for CA-MRSA skin infection?

- HIV-positive
- Lives in a crowded living situation
- Possibly poor hygiene

How will Ferdi prevent others in his group home from getting infected?

- Finish all his antibiotics as prescribed.
- Keep the wound covered at all times. Do not allow others to touch the wound.
- Do not share linens or towels or other personal items with others.
- Wash hands thoroughly.

ings in the skin (such as cuts), contact with contaminated items, crowded living conditions, and poor hygiene.

What type of infections does CA-MRSA cause?

"Staph" bacteria are one of the most common causes of skin infections in the United States. The majority of MRSA infections occur in patients in the hospital, but it is becoming more common in the community.[1]

Most commonly, CA-MRSA causes skin infections that may look like a pimple or boil. The skin can be red, swollen, and painful and can have pus in it. Patients often say it looks a spider bite. Staph infections can also cause more serious infections such as blood stream infections, urinary tract infections, or pneumonia. If you think you have a staph infection, it is important to contact your healthcare provider.[1]

How are these infections treated?

Skin infections caused by MRSA, such as boils and abscesses, may be treated by incision and drainage of the wound by your healthcare provider. Antibiotics may also be used along with draining the wound. Often times, a biopsy of the skin or drainage from the infected site are sent to a microbiology lab in order to determine which antibiotic will be effective against the bacteria. For the HA-MRSA infections, a limited number of antibiotics are effective, so an intravenous antibiotic (an antibiotic given through your veins) called vancomycin can be used. CA-MRSA has unique susceptibilities in that more oral antibiotics are effective against it. To make things more complicated, CA-MRSA, like all bacteria, can be different strains in which varying antibiotics will be effective. For example, the strain of CA-MRSA that infects one person may be susceptible to antibiotic A and not to antibiotic B, but the strain that infects someone else might be cured with antibiotic B and not A. This is an important reminder that having your healthcare provider get a culture (or biopsy) is important for effective treatment.[1,5]

Which antibiotics can be used against CA-MRSA?

There are several oral antibiotics that can be used against CA-MRSA. Luckily, Bactrim (generic name trimethroprim/sulfamethoxazole) is effective in those bacteria that are susceptible. This is the same drug that is used for PCP prevention in patients with CD4 counts less than 200 cells, but a higher dose is needed to treat the skin infections. Clindamycin is another antibiotic that can be used, but some strains of CA-MRSA may be resistant to it. It is a good alternative for those who may be allergic to "sulfa" antibiotics like Bactrim. Another group of antibiotics that can be used include doxycycline, minocycline, and tetracycline. Lastly, oral linezolid can be used, but it can be more expensive and reserved for special circumstances. Sometimes rifampin (a well-known tuberculosis

drug) can be used in combination with another oral antibiotic for treatment. If a serious infection occurs and hospitalization is required, intravenous antibiotics may be needed, such as vancomycin, daptomycin, quinapristin/dalfopristin, linezolid, or tigecycline, or the intravenous forms of Bactrim, clindamycin, or doxycycline.[3]

CA-MRSA is transmitted from person to person via contaminated hands, and sharing towels, clothing, sports equipment or personal hygiene items (such as razors).

Rupali Jain, Pharm.D., BCPS, is a Clinical Associate Professor at the University of Illinois at Chicago Medical Center, specializing in HIV care pharmacy. She also updated Positively Aware's 2007 Annual HIV Drug Guide. She thanks Dr. Mandavi Kulkarni for her review of this article and helpful comments.

How do I prevent CA-MRSA skin infections?

As mentioned earlier, CA-MRSA is transmitted from person to person via contaminated hands, and sharing towels, clothing, sports equipment or personal hygiene items (such as razors). Other factors contributing to transmission include skin-to-skin contact (for example during contact sports), crowded living conditions, and poor hygiene. So in order to prevent these infections follow these simple steps:

1. Keep hands clean by washing them thoroughly with soap and water. (You can also use alcohol-based hand sanitizers.)
2. Keep cuts and scrapes clean and covered with a bandage until fully healed.
3. Avoid contact with other people's wounds.
4. Avoid sharing personal items such as towels, razors, or sporting equipment without proper disinfection.

The above principles also apply to people with staph infections who do not want to infect others. [1]

What happens if the infection comes back?

Sometimes the staph or MRSA skin infection comes back after it is cured. To prevent this, it is important to follow the treatment plan given by your healthcare provider. It is important to take the antibiotics (if prescribed) until they are finished even if your wound looks better after several days. It is also important to follow the prevention steps outlined above. Contact your healthcare provider if the infection is not getting better in a few days. [1]

What do I do if I think I have a MRSA skin infection?

Contact your healthcare provider if you think you may have a skin infection.

Although some of the above information about CA-MRSA infections seems scary, it is important to follow the simple prevention steps outlined above and contact your healthcare provider if you think you may have an infection.

For more information go to the Centers for Disease Control and Prevention website: http://www.cdc.gov/ncidod/dhqp/ar_mrsa.html.

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A New Approach: Immune-Based Treatments against HIV

by Daniel S. Berger, MD

It may be impractical to attempt maintaining patients on life-long antiviral pills, especially since the evolving problem of resistance is not going away. With each passing year, more patients eventually develop resistance to their antiviral cocktail and a new regimen must be constructed. One does not ignore the mounting cost of these medications and their long-term side effects. Some patients are not able to adhere to their medication schedule. Regardless of the cause, viral resistance continues. As virologic failure occurs, the immune system is one of the first things to be affected, specifically CD4+ T-cells which begin to decline. If untreated or ignored, it can lead to feeling unwell and various complications can develop. It would be advantageous to upgrade and improve the immune system and its function, so that it helps fight the virus on its own terms and/or keeps antivirals working longer. Don't rule out the fact that if the immune system is able to fight HIV, antiviral drugs would not always be needed. This is the basis for developing therapies that improve immune response.

HIV meds, such as protease inhibitors, nucleoside inhibitors, and the upcoming integrase inhibitors act on the virus to reduce replication. Through an indirect mechanism of removing the offending virus, the immune system is facilitated to repair itself. Presently, antivirals are the mainstay of treatment for HIV infection. In the case of immunotherapy, treatments are designed to *directly* and effectively stimulate an immune response against HIV.

I believe that the field of immunotherapy is a sleeping giant. An example of the successful use of immune therapies can be seen with interleukin-2. Interleukin-2 stimulates the immune system to attack cancer tumors and is currently approved for metastatic kidney cancer and metastatic melanoma (a form of skin cancer).

It has also shown to be of value in increasing T-cell counts in HIV disease and perhaps limiting HIV replication, by way of its immune-stimulating characteristics.

The focus of this article is to rivet the eye: imagine the new work being conducted in the front yards of Chicago specifically at Northstar Healthcare, a progressive HIV treatment and research center devoted to care of patients with HIV. The reader will get an inside peak at how different and novel approaches are being tried. However, make note that the ongoing research of the various new antiviral targets such as integrase and entry inhibitors will not be discussed here, as they have already been written about in other recent installments of "The Buzz." Finally, in the face of progress with new inhibitors, there have been no signals that pointed to a cure for HIV. Perhaps immune-based approaches may lead us closer to this goal.

I believe that the field of immunotherapy is a sleeping giant.

A therapeutic vaccine

We hope to be participating in a new project of immunotherapy, developed in Norway. The field of immune-based therapy is based on the premise of directly and effectively stimulating an immune response, so that the immune system components being generated can fight off HIV. In regards to this treatment vaccine, it is peptide (protein chain) based and previous study has shown significant benefit by slowing the deterioration of CD4+ T-cells after this treatment was applied to HIV-positive individuals. The current design is as follows: participating patients will be immunized or vaccinated while on their HIV medication. The continuation of HIV treatment keeps the virus in check while the immunization will take root. At a point later during the study, patients will stop their HIV meds for a short period so that the re-emerging HIV can stimulate an immune response being instigated by this vaccination. Patients will then again restart HIV meds for another short period to allow for protection of the immune response that is expected to go into high gear. Patients will then stop a second time, this time for a long period. We are hopeful that each individual mounts a response to the vaccine, sees a reduction in the decline of T-cells and has the potential for safe and prolonged time periods off of HIV meds.

New Zealand goats

Another type of immune-based treatment study starting at Northstar is being developed in New Zealand. This type of immune treatment belongs to the area called passive immunotherapy. This refers to the passive transfer of immune fighting cells to an individual with a compromised immune system. As another example of passive immunotherapy, some patients at Northstar get an intravenous infusion of IgG antibodies to various bacteria and viruses to protect them from infections and other complications.

In this study patients with T-cells below 200 will get infusions of antibodies to HIV that will be harvested from goats who were exposed to the virus. It is in the beautiful rolling hills of New Zealand that these goats are found and bred. Importantly, the specific transfer of antibodies are of the polyclonal type. Polyclonal antibodies are created with multiple B-cell (immune cells that produce antibodies against infection) clones and are felt to be very effective compared to monoclonal antibodies (being of one cell line) which are not.

Why animals and why goats? As humans, if we get exposed to animal-related viruses, we do not get sick; conversely, animals getting exposed to human viruses including HIV also do not become ill with the disease. The goats mount a unique immune defense against HIV, producing antibodies to distinct regions of the virus which are dissimilar to the antibodies that humans can accumulate and develop. An observation showed that goat antibodies are sensitive to different parts (regions) of HIV, called epitopes, for which the human immune system ignores. (An epitope is a portion of a molecule to which an antibody binds).

The discovery of new epitopes on HIV and the new technology that is being used to stimulate antibody production against these new found epitopes make for a novel and alternate target for which to fight HIV. Possible side effects to receiving goat-derived antibodies are various allergic and hypersensitivity responses to the treatment. Because this treatment is being offered to individuals with T-cell counts below 200, it is felt that this problem will be minimized. Patients will be given this treatment by intravenous infusion at Northstar three times weekly for 16 weeks.

First in class mutagenesis drug

An additional novel treatment proposes to treat patients who harbor multi-drug resistance to HIV. The treatment is borne out of genetic testing of the virus. The discovery of other genetic components of HIV has led to another target for treatment. The mechanism or how the drug works is that the medication gets incorporated into the HIV gene. The result is a uniquely mutated HIV that changes its ability to stay viable (alive), what is referred to as viral decay. This study is in early-stage work and we are hopeful that this forms a basis to rid the body of replicating virus, and possibly virus that is in the dormant (or inactive) stages.

Summary

These are very exciting times in HIV research while we take advantage of the new technology. The studies described in this article are not intended to discuss results of treatment nor how they might compare with other therapies. Instead, as is often the case, the purpose of this column is usually to discuss evolving research and new trends in treatment. Today these newly invoked treatment paradigms look quite promising as a hypothesis coming to the research-focused clinic.

To what degree an immune-based therapy will become a significant addition to treatment is still unknown. However we must continue to search because if we don't look, we will not find. Thus as an early window's view into the future, we continue to remain on the cusp of the research. As progress continues, treatments of the future will be reshaped; they will not look like the present. Already, integrase and CCR5 (entry) inhibitors are expected to be approved shortly and will surely change our approach to treatment. We strive for ways to improve HIV therapy from different vantage points. Immune therapy and other treatments continue to evolve.

Daniel S. Berger, MD, is the founder and Medical Director of Chicago's largest private HIV treatment and research center, NorthStar Healthcare and Clinical Assistant Professor of Medicine at the University of Illinois at Chicago. Dr. Berger serves on the Medical Issues Committee for the State of Illinois and the Board of Directors for the AIDS Foundation of Chicago. Dr. Berger can be reached at DSBergerMD@aol.com or (773) 296-2400.

Sweet Release

An exercise for letting go of negative energy

by Sue Saltmarsh

I have a candy jar on my desk. In the course of a day, quite a number of TPAN staff members and volunteers stop by to grab an Almond Joy, a Twix,or some Laffy Taffy, most of them muttering self-judgmentally about their lack of will power and other such conditioned twaddle. As they stand picking through the bowl for their preferred treat, I have a chance to have some (usually humorous) exchange and, occasionally, to ask them how they're doing if I notice their energy feeling heavy, dark, or frantic. It was one of those opportunities that inspires this column.

One of the physician's assistants at the clinic reached into the bowl with a deep sigh and his energy felt like the weight of the world. It had been "one of those days" that occur on a regular basis for those who work with people who are physically ill, emotionally traumatized or otherwise needful of help in some way—a day when we feel bombarded by the pain and despair of others to the point where we carry it with us. I was guided to share with this compassionate man a "spell" or ritual that I'd developed during my years of doing energy work at another agency.

I would frequently see people there who lived lives of such struggle, such pain that it was hard to believe they survived. It was a blessing on the one hand because, compared to what they dealt with, my life was a piece of cake! But it was also a challenge because I had to find some way to honor my concern for them and yet not take on their problems, their lessons as my own.

Back then, I had a 45-minute commute, during which I would use the time and solitude to regain my balance, to get back to the center I'd been knocked off of, to release my clients with love and gratitude for what they constantly taught me. I hoped it would help my colleague not to take that heavy energy home with him and since that day, he's honored me several times by telling me how much it has helped him.

As I tried to think of a topic for my column that would fit in with this issue covering CROI, it occurred to me that during those days of sharing reports, statistics, research, experiences, and ideas, the attendees at the conference probably also shared each other's frustration, anger, grief, and fear. The combined energies of thousands of people coming together for this mutual, positive purpose and then exchanging not just the positive, but also the difficult energies of the cause, seemed overwhelming to me. I thought about my fellow TPAN tribe members Matt, Jeff, and Enid, and wished I'd given them each a laminated card with this printed on it. So here, for the next big conference, for the next hard day, for the next sleepless night, for *you*, whenever you need it, is my spell:

Take 3 deep, cleansing breaths
Say, aloud, "I release all energy
that is not my own
and does not serve me."
Take 3 more breaths
Say, aloud, "I release all energy
that IS my own
and does not serve me."
(Because we all generate our own negative energy as well as picking it up from others.)

Visualize the top of your head opening up and all of whatever you need to release flowing, tumbling, shooting out to wherever it must go for its highest healing. And know that you have the right and the power to do this FOR YOURSELF whenever you need to.

For those of you battling HIV/AIDS or any other physical illness, send out the physical symptoms too. Release the headache, nausea, diarrhea, neuropathy, sinus infection, fatigue. No, this surrender is not going to cure you, but it doesn't counteract your meds, defy your doctor or harm you in any way. What do you have to lose besides the few minutes it takes to breathe, speak, and visualize getting rid of those things that hold you back or drag you down? Wouldn't it be worth a try if pain was eased, your appetite came back, and you could breathe easier? This is one pro-active way to help yourself. While much has been made of the body/mind/spirit connection and the ways in which it has been shown to help healing, not many people develop it or exercise it consistently. But if the idea that you have something to say about what is and is not in your life, in your body, in your mind and heart appeals to you, maybe you'll find this little ritual of release as helpful as I do. If so, pass it on. This is a difficult world to live in and I believe we can all use a little magic. And for heaven's sake, quit beating yourself up for grabbing a Hershey bar every now and then!

Oh, and thanks, Terry.

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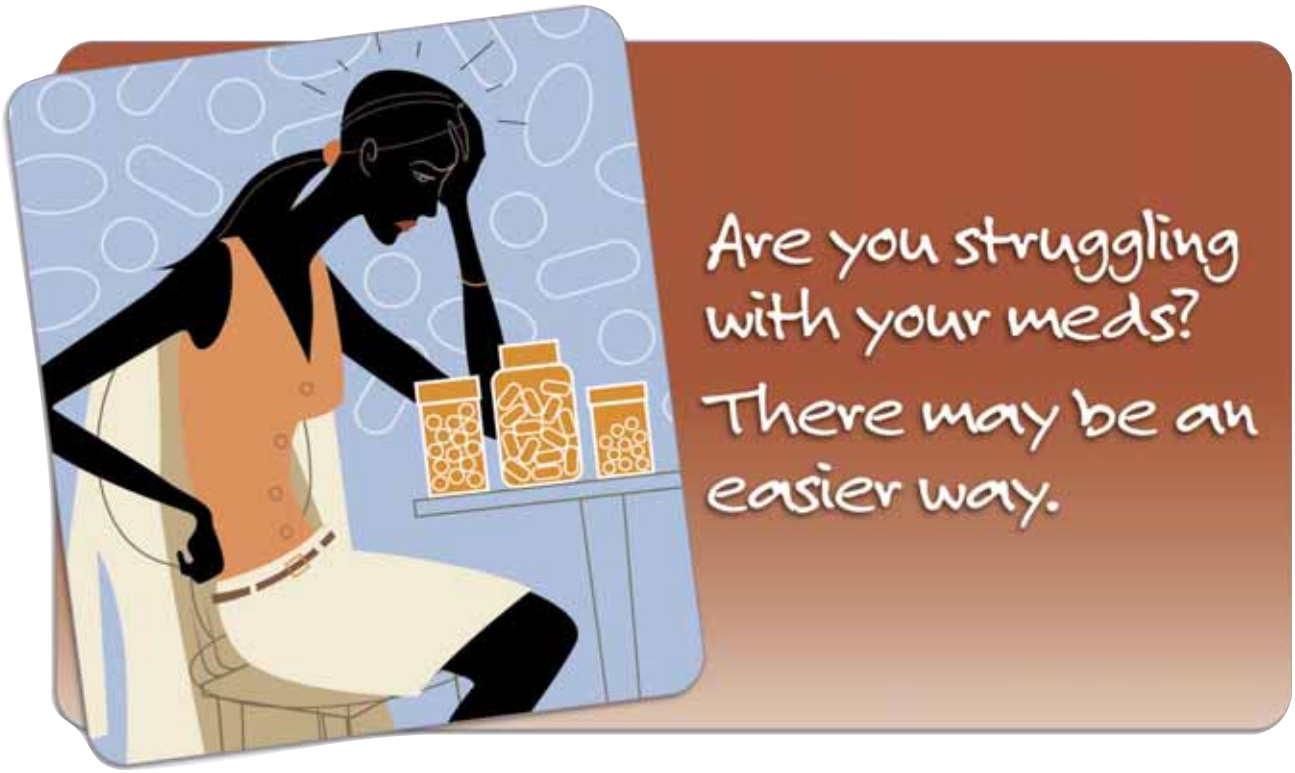
Don't lose yourself to your meds HIV.



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

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- Confidential one-on-one counseling and support
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- Refill reminders to help ensure you follow your medication therapy as prescribed
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