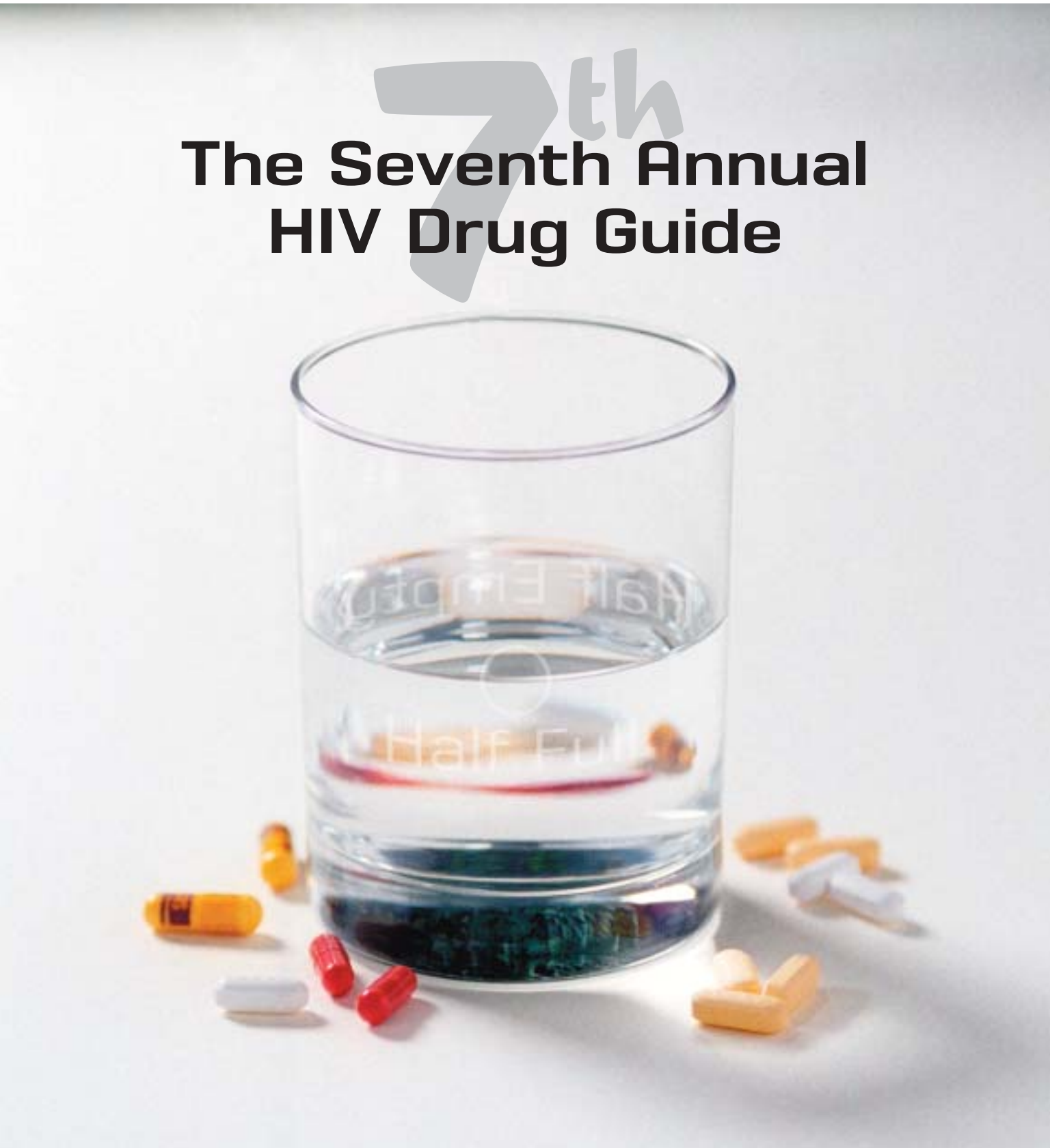
January / February 2003

Positively Aware

The Journal of Test Positive Aware Network

The Seventh Annual HIV Drug Guide



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PAGE
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SUSTIVA
P.I.
PAGE
HERE

Table of Contents

January / February 2003 • Volume 14 Number 1

Departments

20 Editor's Note
2002 in Review—2003 in Preview

26 Readers' Forum

28 News Briefs
by Enid Vázquez

69 The Buzz
The Ever-Changing HIV Treatment Landscape
by Daniel S. Berger, MD

71 Radical Red
Liberation Theology
by Laura Jones

72 Medicine Chest
Combination Dosing Adjustments
by Glen Pietrandoni R.Ph.

75 Pickett Fences
Can You Feel What I Feel?
by Jim Pickett

77 TPAN Calendar of Events

78 TPAN Programs

Articles

32 Moving Forward in HIV Medicine
by Jonathan Uy, MD

34 What's on the Horizon?
by Charles A. Nelson

36 The Seventh Annual HIV Drug Guide
by Charles E. Clifton and Enid Vázquez
Contributing Editor: Patrick Clay, Pharm.D., HIV Clinical Specialist, Kansas City Free Health Clinic; Assistant Professor, University of Missouri at Kansas City School of Pharmacy

40 2003 HIV Drug Chart

61 Drug Prices
by Enid Vázquez

63 Behind the Frontline—A doctor looks at combos & side effects
Interview by Enid Vázquez

66 Positively Aware 2002 Index
compiled by Jeff Berry

73 Combination Drug Chart
Compiled by Glen Pietrandoni, R.Ph.

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

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

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Editor's Note

2002 in Review—2003 in Preview

Depending on whether you see the glass as half-full or half-empty, 2002 was either a promising or a disappointing year for antiretroviral therapy. Viread and Kaletra continued to demonstrate strong potency and limited side effects in on-going follow-up studies. Sustiva became even simpler to dose. Several experimental drugs—T-20, FTC, 908 and atazanavir—moved further along in clinical trials and some moved into expanded access. And my good pal and HIV-pos treatment advocate Dawn Averitt gave birth to a beautiful and healthy daughter. Guess which glass I'm looking at.

Updated treatment recommendations were published in 2002. The guidelines discuss when to begin therapy, what initial regimens to use, treatment interruptions, and monitoring and changing therapy. They are available at http://www.ama-assn.org/special/hiv/hivhome.htm and in English and Spanish at www.hivatis.org. Included in this year's Drug Guide are several charts and tables, which we hope will assist you in talking to your health care provider and HIV specialist about antiretroviral combinations.

Some very helpful websites (in alphabetical order):

- AEGIS: www.aegis.com
- AIDSmap: www.aidsmap.com
- The Body: www.thebody.com
- Gay Men's Health Crisis: www.gmhc.org
- HIV and Hepatitis Information: www.HIVandHepatitis.com
- National AIDS Treatment Advocacy Project: www.natap.org
- The New Mexico AIDS InfoNet: www.aidsinfonet.org
- PositiveWords: www.positivewords.com
- Treatment Information: (HIV positive owned and operated): www.AIDSmeds.com
- Women Alive: www.women-alive.org

Late-breakers

The CORE Center of Chicago reported in Barcelona that deaths due to AIDS after HAART decreased by almost half for their patients between 1996 and 1998. However, for women, and especially African American women, the death rate began to go up again. The increase was 35% for women, and 51% for African American women. CORE Center researchers suggests that local and national research should look at the following issues: late diagnosis, limited access to health care services or limited use of health care services, co-morbidities (other diseases, like hepatitis B or C), adherence and the limitations of current therapies. From 1998 to 2000, deaths continued to go down for men and have since leveled off. The CORE researchers reported that this was also true for national numbers in 1999—there was a plateau, overall, across the country, after a dramatic drop in 1996.

Also from Barcelona, there was information from the University of California at San Francisco showing that HAART did not decrease the rate of a precursor to anal cancer in men who have sex with men (MSM). Researchers noted that the incidence of anal cancer is 37 times higher for HIV-positive MSM than for all men. HAART has been shown to reduce the incidence of *Kaposi sarcoma* and non-Hodgkins lymphoma, but anal intraepithelial neoplasia 3 (AIN 3)—basically abnormal cells that could become cancerous if not treated—was almost three times higher in the positive men on HAART than for the positive men who weren't on HAART. The T-cell count didn't make a difference. Researchers pointed out that AIN 3 takes several years to progress and recommended screening for all positive MSM. The UCSF group looked at here was made up of 433 men.

In the first large-scale trial of its kind (1,200 participants), the "2NN" trial is a 48-week randomized clinical trial comparing the efficacy and

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Editor's Note continued

continued from page 20

safety of Viramune (nevirapine) and Sustiva (efavirenz) in treatment-naive patients, with a viral load greater than 5,000 copies, including a substantial number of patients with viral loads over 100,000, and any CD4 T-cell count, each in combination with Zerit + Epivir. In addition to comparing Viramune (twice daily) vs. Sustiva (once daily), 2NN also compares once-daily vs. twice-daily Viramune and evaluates the efficacy of a double NNRTI combination of Viramune + Sustiva (presented at the 6th International Congress on Drug Therapy in HIV Infection [November 17-21, 2002, Glasgow, UK] and reported by www.hivandhepatitis.com). Secondary objectives include comparing the number of participants achieving a viral load below 50 copies at week 48 between the four study arms; comparing changes in CD4 T-cell count over 48 weeks between the four study arms; and comparing the tolerability of the four treatment arms.

In a decision that outraged HIV treatment advocates around the country, Chiron Corporation announced in October its decision to stop clinical development on SILCAAT, a Phase III study for recombinant human interleukin-2 (IL-2, aldesleukin) in individuals with HIV. SILCAAT is the acronym for the Phase III study in patients with low CD4 T-cells counts (between 50-299), who were randomized to receive IL-2 in addition to anti-HIV therapy. Phase II studies had shown substantial CD4 count increases and no negative effect of IL-2 on viral load. Chiron is examining data collected from over 1,000 individuals.

Does anyone take Crixivan full-dose these days? Preliminary 24 week data (from a 48-week study) on 63 participants receiving two 400 mg capsules of Crixivan with two 100 mg soft-gel capsules of Norvir twice a day, and two NRTIs was presented at the 14th International AIDS Conference 2002. Twenty-seven of 63 participants—an unbelievable 43%—discontinued the study by week 24. Kidney stones occurred in 5 of 63 (7.9%). Twenty-six participants are being monitored through 48 weeks (Abstract B10351).

In a 24-week study, the activity of Viread against hepatitis B (HBV) appears to be very promising in a cohort of 6 HIV co-infected subjects for whom Epivir and interferon (IFN) therapy had previously failed. At entry, all patients were taking Epivir or Coviracil and were hepatitis B positive; four had cirrhosis; baseline HBV load was 7.95 log. By weeks 12 and 24, HBV load had decreased by 3.1 log and 4.3 log, respectively. See www.natap.org and www.HIVandHepatitis.com for additional HIV and hepatitis updates.

Sustiva and False Positives

In 2001, Enid Vázquez wrote an article on the occurrence of false positive results for use of marijuana in HIV-positive inmates who were taking Sustiva (efavirenz). As the result of Enid's work and discussions with Bristol-Myers Squibb (the manufacturers of Sustiva), an important label clarification was made. "False positive urine cannabinoid test results have been observed in HIV-negative volunteers who received Sustiva when the Microgenics CEDIA® DAU Multi-Level THC assay was used for screening. Negative results were obtained when a more specific confirmatory test was performed on the same volunteers using gas chromatography/mass spectrometry. Of the three assays analyzed (Microgenics CEDIA® DAU Multi-Level THC assay, Cannabinoid Enzyme Immunoassay [Diagnostic reagents, Inc.] and AxSYM® Cannabinoid Assay [Abbott Laboratories]), only the Microgenics assay showed false-positive results/the other two assays provided true-negative results." The effects of Sustiva on cannabinoid screening tests other than these three are still unknown. The manufactures of cannabinoid assays should be contacted for additional information regarding the use of their assays with patients receiving Sustiva.

Past, Present and Future ADAP Woes

The high prices of antiviral drugs continued to impact us in 2002 and could devastate health care options and public health programs in 2003. At the end of 2002, 13 states already had waiting lists for their AIDS Drug Assistance Programs (ADAP) and seven other states are considering placing limits on the type and amount of antiviral drugs HIV-positive persons can access for 2003. Federal funding for ADAP during fiscal years 2001 and 2002 did not meet the funding needs of many states and U.S. territories, including the U.S. Virgin Islands, Guam, the Marshall Islands, the Northern Mariana Islands and the Commonwealth of Puerto Rico. According to reports, Alabama, Idaho, Indiana, Kentucky, Montana, Nebraska, North Carolina, Oregon, South Dakota, Texas, Wyoming, Washington and Guam are currently struggling with waiting lists, closed programs and drug access restrictions.

A major factor in ADAP shortfalls over the last three years is the increasing cost of medication. High drug prices also have had a negative impact on insurance premiums and co-pays for prescription drugs. Many states are attempting to avoid the same budget shortfalls by limiting the number of drugs on the plan, decreasing financial eligibility to 200 percent of the poverty level, having a 90-day waiting period for program enrollment for new state residents and looking into price breaks on drugs from pharmaceuticals. Cut the cost of the drugs. What a novel idea.

States expected to have waiting lists and restricted access in early 2003 include Colorado, Florida, Georgia, Nevada, New York and South Carolina, as well as the U.S. Virgin Islands. Remarkably, the entire southeastern region of the United States, with some of the lowest annual incomes and highest rates of HIV, is represented in the list of states with (nearly) bankrupted ADAPs. It's past time to make your voices heard.

New Year Babies

Enter Fuzeon (T-20), the first drug from a new class of anti-HIV drugs called "fusion inhibitors." What are fusion inhibitors? Simply put, Fuzeon prevents HIV from attaching to the host cell, thereby preventing the virus from entering the cell and beginning its replication process. It is expected to be widely available by March 2003. Although no price has been set by its manufacturer, Roche-Trimeris, the hot buzz in the treatment community is that Fuzeon is expected

continued on page 27

Readers' Forum

Positively Aware will treat all communications (letters, faxes, e-mail, etc.) as letters to the editor unless otherwise instructed. We reserve the right to edit for length, style or clarity.

Write to: Positively Aware,
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E-mail: readersforum@tpan.com

Hep C

I have been receiving your mag now for three of your 15 years and wanted to share my experience with being HIV co-infected with hepatitis C. My doctor had my viral load for hep C undetectable for over 15 months. The doctor gave me the option to go off therapy. And of course I took that option. Interferon is not a very fun drug, but which drug is in this world? So now after four months of being off therapy, my hep C viral load is still undetectable. He recently informed me that I am in the 90% window period for purging that virus from my system. I dare not use the "cured" word. Please visit my wife's Web page, www.angelfire.com/ky/zoezone/. Thank you. Good luck to all soldiers in this war!

Michael Trauth,
via the Internet

Neuropathy

(Addressed to Dr. Dan Berger) I enjoyed your article in *Positively Aware* this month (The Buzz, November/December 2002). I did want to bring up two issues around your comments. First, regarding B-6: it is important that the client not take excessive amounts of B-6 as this can cause or worsen neuropathy. Secondly, I have found B-12 (injectable and/or sublingual), either alone or in conjunction with B-6 and folic acid, to be very helpful in decreasing neuropathies. John Senneff has written some wonderful guidelines for HIV neuropathies. In particular you may find Senneff's *Nutrients for Neuropathy* very interesting reading.

Heather Johnstone, Ph.D., RN,
via the Internet

Dan Berger replies: Dr. Johnstone, I appreciate your comments. You are right about vitamin B-12. I forgot about mentioning that, probably because I have virtually all my HIV-positive patients getting B-12 injections during their routine visits to the clinic. B-12 is quite innocuous and has many potential benefits—hematologic, cognitive, and anxiolytic, to name a few, as well as with peripheral neuropathy. Thanks for pointing this out. On the subject of B-6—I didn't mention dosing but you're absolutely correct about potential toxicity. In a study of women being treated with vitamin B-6 for PMS [premenstrual syndrome], new onset peripheral neuropathy was reported. It is associated with prolonged and continuous administration. In treating patients with HIV-related peripheral neuropathy we typically use lower dosing, generally about 25 mg per day, but sometimes 50 mg, and we are careful to not continue for too long. Also, I have some patients taking it on "every other day" dosing schedules. Thanks again for taking the time in writing me.

Lipodystrophy

Do you have a support group for HIV-positive men with metabolic disorders? I have been positive for at least 17 years and have never had any problem dealing with that. But drug side effects are a separate, and for me, much more difficult issue. If you don't have any relevant program, maybe you could refer me to another source; or maybe your current programs could be expanded for the "metabolically challenged."

I live in Chicago. Thanks.

Name withheld,
via the Internet

Editor's Note: Although this reader wrote to our Programs Department, I wanted to take this opportunity to let our readers know about a lipodystrophy group online. Visit http://groups.yahoo.com/group/lipodystrophy/join. —Enid Vázquez

One Bad Apple

In 2001 I wrote a letter entitled "Double Damned." As a result of that letter I received much support from outside sources and other people with HIV. I greatly appreciated both the criticism and concern. It made me a better person and made me realize that each experience with HIV is different and we all have our individual fears. Sometimes those fears turn us into our own doctors and we believe that the men and women treating us harbor some kind of secret agenda apart from our best interest, especially in prison. I wrote a sweeping statement condemning all of the hardworking doctors and other healthcare workers. I apologize for labeling these good people. I am not saying that I haven't had bad experiences, but I can't say that one bad experience tainted the entire institution. I will be going back into society soon and wanted to clarify my earlier comments.

Larry Harris, Dixon Correctional,
Dixon, Illinois

Talkin' 'bout My Generation

Please tell Mr. Weeks: "Thank you." I have just read his article (Nov./Dec. 2002). As a 30-year-old recently pos gay guy in the Midwest, I can identify strongly with his

Editor's Note continued

continued from page 25

to enter the market as the highest-priced anti-HIV drug ever. Oh, baby!

GlaxoSmithKline is developing a pro-drug "908" (new version of Agenerase), with a lower pill burden and improved tolerability. Data presented on the NEAT Study (GW433908) in 2002 compared the efficacy, durability and safety of 908 to Viracept (nelfinavir), both in combination with Ziagen (abacavir) and Epivir (3TC), in treatment naïve individuals. At this point both regimens demonstrated comparable gains in CD4 T-cells counts and decreased viral load. The edge with the pro-drug 908 is that it demonstrates greater potency in individuals with higher viral loads (over 100,000 copies) and a much lower incidence of diarrhea. Triglycerides were also lower in the 908 arm of the study, but that won't mean a thing if 908 is eventually paired with Norvir, in attempts to produce a once-a-day drug. The 908 drug could very well gain FDA approval in 2003.

And with Coviracil (FTC) and atazanavir both expected to enter the antiretroviral market at some point in 2003, something has got to give or the ADAPs coast-to-coast are going to go bust, leaving potentially thousands of individuals out in the cold.

Bush-whacked?

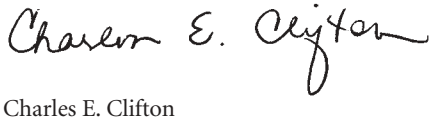
In July at the 14th International AIDS Conference, in Barcelona, the U.S. Secretary of Health and Human Services announced (although no one could hear him), "the fight against HIV/AIDS has no greater ally than the United States under President Bush. Therefore, it is time we all work together as partners to end this terrible scourge that is tearing apart families, communities and, yes, even countries." Some HIV advocates contend that President Bush is on target to do more for attempts "to finding a cure and an effective vaccine" than any administration. However, many believe that the Bush domestic policies on HIV care and prevention are threatening the lives of thousands of HIV-positive citizens, and of advances made previously to rid our society of the stigma and discrimination attached to this disease. In 2003, make the Bush administration officials and local comminity leaders demonstrate a real commitment to assure quality and expanded health care services, to address the crisis in ADAP, housing, and mental health services for people living with HIV, and to support science-proven HIV prevention practices (Mr. Thompson's speech is printed in its entirety in NUMEDX July-Dec, 2002, www.numedx.com).

A slam dunk Tarheel style

Hats off to a remarkable group of people in the "Triangle" of North Carolina. In the aftermath of what was probably the worst ice storm in the history of Raleigh, Durham and Chapel Hill—a storm which left the area literally paralyzed with no electricity or heat and with temperatures below freezing for days—this community of compassionate and caring individuals, lead by the Alliance of AIDS Services-Carolina, pulled off a remarkable AIDS Walk. I had the honor of being the keynote speaker at this event. And while many of my hosts were themselves "homeless" from the storm, they provided me with the best in Southern hospitality. And even more warming to my heart, on a cold December day, was the tremendous show of support from the faith-based organizations in the area. I know of many churches and religious and political "leaders" from around the country and my hometown of Chicago who could really learn from what you guys are doing. Way to go!

Finally

Special thanks go out to a number of individuals who have been vital not only to the production of the 2003 Drug Guide edition of *Positively Aware*, but to the overall success of this publication—Enid Vázquez, Jeff Berry, Russell McGonagle, Patrick Clay, Charles A. Nelson,Jonathan Uy, Kristin Lee, Daniel Berger, Glen Pietrandoni, Jim Pickett, Laura Jones, Matt Sharp and Carlos A. Perez. And lastly, thank you Kurt, Carlisle and Cassie (and the spirit of Tina) for sharing me with so many people.



Charles E. Clifton
Executive Director / Editor
Send comments and reactions to ed@tpan.com

Readers' Forum continued

reflections. Please tell him thanks for voicing his thoughts. Fight hard!

Name withheld,
via the Internet

"What next? What do I do now? I want to be an activist, I want to protest, I want to scream and be heard. What's this generation going to do now?" Scream bloody murder about the epidemic level of HIV in communities of color, especially among young black and Latino Men Who have Sex with Men (MSM). About the fact that African-Americans make up 12% of the population and 50% of new AIDS cases. Scream bloody murder about the lack of resources for culturally competent HIV education/prevention programs. Scream bloody murder about the lack of resources for treatment in minority communities. Scream bloody murder about the fact that African American women make up a truly absurd percentage of infections among all women... something on the order of 60%. The truth is that this is where the greatest problems are. In all likelihood, we are going to lose an entire generation of young African-American and Latino men [*and women—Charles Clifton*]. It's racism, pure and simple, in its most deadly form.

Thomas Leavitt,
via the Internet,
http://www.thomasleavitt.org/cc

News Briefs

by Enid Vázquez

Videx warning

Using the hepatitis C drug ribavirin increases blood levels of Videx and Videx-EC (didanosine, ddI), and therefore may increase the risk of serious side effects. The U.S. Food and Drug Administration (FDA) in September added a warning to this effect to the package insert for Videx (that folded up piece of paper that comes with medication), following case reports and information published in the medical journal *The Lancet*. Time to toxicity was about five months. The warning (printed in bold) reads, "Co-administration of ribavirin with Videx should be undertaken with caution, and patients should be monitored closely for didanosine-related toxicities. Videx should be suspended if signs or symptoms of pancreatitis, symptomatic hyperlactatemia, or lactic acidosis develop." (See the HIV Drug Guide).

Videx EC/Viread

A tiny pharmocokinetic study found good news. Videx EC taken at a lower than normal dose (250 mg) is equal to the standard 400 mg dose when taken with Viread. This was true with or without food. Knowledgeable practitioners were already prescribing the 250 mg Videx dose because of the increased blood levels when taken with Viread. This can lead to increased toxicity (see above).

Metabolic guidelines

Finally, comprehensive information about the metabolic abnormalities being seen in people on HIV therapy. A volunteer panel of experts brought together by the International AIDS Society-USA produced the 18-page report (which is written for healthcare providers). The guidelines for clinical management include details on what's known so far regarding these conditions as they relate to HIV: insulin resistance with alterations in glucose metabolism; abnormalities in lipid metabolism; lactic acid disorders; bone disease and abnormal body fat distribution. According to a press release from the University of San Francisco, "These metabolic complications are troubling—high cholesterol and blood glucose levels may increase the risk of heart disease and stroke. Lactic acidosis is a potentially fatal disorder." Panel chair Dr. Morris Schambelan is a professor of medicine at the university. The recommendations, published in the November 4 issue of the *Journal of Acquired Immune Deficiency Syndromes* (JAIDS), is available from www.iasusa.org.

Hep B drug

Hepsera (adefovir dipivoxil) was approved late last year by the U.S. Food and Drug Administration (FDA) for treatment of hepatitis B. Larry Kramer, a prominent playwright and activist living with AIDS, went before the FDA to credit the drug with "saving" his life while he waited for a liver transplant, and almost called off the surgery. Kramer, a founder of ACT UP (AIDS Coalition to Unleash Power), received no financial backing or incentive from the maker of Hepsera to make his presentation.

But HIV specialists are wary about using Hepsera in their positive patients. The drug had earlier failed to get approval as an HIV medication. Now it has approval for hep B treatment at a much lower dose. Promoters say that low-dose Hepsera is not enough to cause drug resistance to Epivir or Viread, two HIV drugs that also have hep B activity. Docs aren't so sure—and many aren't willing to risk having their patients develop resistance to the two important HIV meds. On page one of the drug's package insert is a warning about the development of HIV resistance in people with unknown or untreated HIV. The National Institutes of Health (NIH) is looking at whether low-dose Hepsera might cause cross-resistance to HIV drugs. Hepsera has been found to provide benefit for people whose hep B has developed resistance to Epivir-HBV, which is also used at a lower dose than its HIV

treatment as Epivir. On-going studies are looking to see if Hepsera causes kidney damage beyond a year of use (the amount of study time upon which the FDA approval was based). Around 5% of people in clinical trials showed signs of kidney toxicity after a year. The study of Hepsera in people with HIV is minimal.

Positively Aware medical advisor Dr. Daniel Berger points out that most hepatologists know of Hepsera, but have little experience or are currently unfamiliar with Viread. Dr. Berger reported that, "Data from a prospective pilot study in patients who are co-infected with HIV and hepatitis B, who previously failed interferon and Epivir therapy, was recently published. The study, in the December 15th issue of the *Journal of Infectious Diseases*, showed effective suppression of hepatitis B by tenofovir consistent with previous retrospective data abstracted from clinical trials presented at two national and international conferences. Tenofovir offers more advantages over that of Hepsera for co-infected patients. First, adding adefovir can pose further toxicities to patients on existing and complicated HAART regimens. Second, 10 mg Hepsera is not fully suppressive for HIV, therefore adding the risk of possibly developing HIV resistant mutations. Finally, tenofovir's safety, tolerability and effectiveness against both viruses has been sufficiently demonstrated. Patients who are co-infected with HIV and hepatitis B can be offered effective treatment for both viruses using tenofovir."

Crypto drug

The FDA in December approved Alinia (nitazoxanide) for treatment of children with diarrhea due to *cryptosporidium* or giardia (both parasites found in contaminated water). The oral suspension is the first medicine approved for crypto. If left untreated, the severe diarrhea it causes can lead to death in people with AIDS. Outbreaks have taken place in day care centers, swimming pools, water park wave pools and public water supplies. The manufacturer says Alinia comes in a "pleasant-tasting, easy-to-use liquid suspension form," taken for three days. The company also said that side effects were not significantly different from placebo (fake drug) and included abdominal pain, diarrhea, vomiting and headache. The company filed for approval of tablets for adults and for treatment of cryptosporidium-induced diarrhea in AIDS patients.

Nix N-9 lube

The Global Campaign for Microbicides issued a "Call to Discontinue Nonoxynol-9 for Rectal Use." Campaign materials report that, "N-9 is the active ingredient in over-the-counter contraceptive products sold in the U.S. and elsewhere and is added in smaller amounts to some sexual lubricants and to the outer surface of some condoms. …the Call was developed to address the fact that many individuals are still seeking out and using lubricants and condoms containing Nonoxynol-9 in the mistaken belief that they offer added protection against HIV and STDs. In fact, these products may increase the user's risk of infection." Although rectal use was singled out because of the higher risk of transmission, N-9 may also irritate the vagina, thereby increasing risk. The campaign also called for manufacturers to stop adding N-9 and for stores to stop selling products with N-9. Last year, the World Health Organization (WHO) issued a Consensus Statement noting that research definitively shows that N-9 does not prevent HIV or STD transmission.

Vitamins and infant transmission

Multi-vitamin pills may reduce the risk of HIV transmission from a pregnant woman to her infant, and improve the child's health, but vitamin A supplementation by itself may increase risk. However, only women with low white blood cell counts had the benefit with the vitamins. U.S. and African researchers looked at 1,100 women, from the 20th week of pregnancy through breastfeeding (in itself a risk for HIV transmission). Dr. Wafaie Fawzi of the Harvard School of Public Health and her colleagues published their report in the September 27 issue of *AIDS*.

HIV is no picnic

That's according to a new ad campaign from the City of San Francisco. For those who thought meds were an easy solution if they get infected, the posters on bus shelters and other spots will show people with unhappy medication side effects—like a huge belly or sitting on a toilet seat (diarrhea).

Another new ad campaign in the city and other parts of the country, part of the ongoing HIV Stops with Me, shows HIV-positive people discussing how they prevent transmission. One person says being rejected doesn't feel as bad as knowing you've infected someone. Visit www.hivstopswithme.org.

New-Fill available

Two U.S. doctors have the investigational device exemption from the U.S. Food and Drug Administration (FDA) that's needed to provide New-Fill to patients. The material is used to fill in cheeks and temples hollowed out by HIV medications. Not yet approved in the U.S., the FDA stopped doctors from using it last year. The doctors are Peter Engelhard in Miami Beach (1–305–534–7255) and Douglas Mest in Hermosa Beach, California (1–310–374–0347). For more information, see an article in the Washington Blade, http://ww2.aegis.org/news/wb/2002/WB021008.html.

Taz access

The experimental once-a-day protease inhibitor atazanavir is available through an expanded access program. The program provides free drug to people on a failing HIV regimen who have more than 5,000 viral load, less than 200 T-cells and no other treatment options, as well as to people with severe HIV drug-related lipid levels that have not been controlled by medication. Doctors can call the program toll-free 1–877–726–7327. See the HIV Drug Guide section for more information.

HIV protection, dementia risk

A mutation in the MCP1 gene lessens the risk of HIV infection by 50%. However, after infection, it seems to increase the risk of dementia by four times. Researchers published their findings in the October 15 *Proceedings of the National Academy of Sciences*. The research was based on blood samples of 1,115 adults with HIV and 592 children exposed to the virus in the womb. Testing for this gene is not available in the doctor's office. For more information, see www.kaisernetwork.org/daily_reports/rep_index.cfm?DR_ID=14187.

Newborns in Argentina

Doctors reported that an HIV prevention program in nine public hospitals in Argentina has reduced the rate of mother-to-child transmission by nearly 90 percent. Pregnant women coming into the Buenos

Aires area hospitals were tested for HIV. HIV-negative women received counseling, while positive women received counseling, HIV treatment and infant formula to avoid breastfeeding transmission. The treatment led to a decreased incidence of transmission to the infants from 25 to 2.7 percent. Of the 144 HIV-positive women in the program, half did not know they had the virus.

Hep C scholarship

The New Horizon Scholars Program offers 50 college scholarships to Latinos and African Americans infected with hepatitis C or who are dependents of someone living with the disease. The deadline is February 15. Students must be enrolling in a four-year college for the first time. Visit www.hsf.net or call 1–866–346–7406).

New rapid HIV test

The FDA in November approved an HIV test that gives results in 20 minutes. However, the OraQuick test can only be conducted by healthcare workers certified to use it, thereby limiting the community settings where it can be taken. Several individuals and organizations, including the President's Advisory Council on HIV/AIDS, called for a waiver to make the test more widely available. OraQuick requires a finger prick and, like a home pregnancy test, gives results by changing colors on a stick (showing one or two stripes). It looks for HIV antibodies, and as is usual with an HIV test, a confirmatory test must be made. It's not the first rapid HIV test, but its accuracy is much better: 99.6%. Many people (the CDC estimates 8,000 annually) fail to return for the results of their HIV test (usually two weeks later), so there's great hope that OraQuick will ease this problem. More people will know of their infection—the U.S. Centers for Disease Control and Prevention (CDC) estimates that one in four HIV-positive people in this country don't know they're infected. This in turn will lower transmission and help lead positive people into appropriate health care.

STD vaccines too

Researchers reported good results with Phase I study of vaccines for the sexually transmitted diseases human papilloma virus (HPV, which is a main contributor to cervical cancer) and herpes. What does this have to do with HIV? STDs increase the risk of HIV transmission. A vaccine would be especially beneficial in poor countries. The reports were published in the November 21 issue of the *New England Journal of Medicine*. Protection against cervical cancer and herpes could also help people with HIV, who progress faster and more severe disease from these viruses.

Valtrex in HIV

Valtrex (valacyclovir HCl) herpes treatment in people with HIV was found to double the time to recurrence of an outbreak. These are preliminary results (six months) from 293 people. This is the first time the herpes med was studied in positive people. The caplets are taken twice a day. The results were compared with a third of the people, who were given placebo. Valtrex side effects included headache, diarrhea, and respiratory tract infection. The study was reported at the annual meeting of the Infectious Diseases Society of America in October.

Viread PEP

The one pill once-a-day HIV drug, Viread, is very well tolerated—and has shown a strong ability to prevent transmission in monkeys. In November the Bill & Melinda Gates Foundation awarded Family Health International (FHI) a $6.5 million, three-year grant for a multinational clinical trial to study the safety and efficacy of Viread (tenofovir DF) in for post-exposure prophylaxis (PEP) in poor countries. Adults regularly exposed to the virus (not explained) will be enrolled in the study. "As an antiviral treatment, tenofovir DF has several characteristics that make it a promising candidate as a method of HIV prevention, including its safety, efficacy, pharmacokinetic and resistance profiles," collaborators reported. Viread is also being studied in the U.S. as a gel microbicide. Anecdotally, one Chicago doctor has an HIV-negative gay male patient who takes Viread because he has anal insertive intercourse with a positive boyfriend (he's the "top" and his positive boyfriend is the "bottom"). The patient asked for Viread after learning about the drug's success with prevention in monkeys. In less than one year of use, as far as his doctor knows, he has not seroconverted, but the patient has not been re-tested recently. The couple does not use condoms. The doctor discussed this approach carefully with the patient and maintains that there was no sufficient basis to recommend this approach to this or any of his other patients.

Currently, the use of HIV drugs to prevent infection after exposure is complicated. There are guidelines for health care workers and in some cases, rape victims. There are also studies in people with sexual exposures. However, two or three HIV medications are the rule, taken for one month, and usually paid for out-of-pocket (about $1,000 for the month). Side effects tend to be difficult. PEP is not to be taken lightly.

Drug discount

TheBody.com has opened an HIV drug co-op. The BodyPlus program offers discounts of up to 45% and free delivery is available on most meds commonly used in HIV. However, people who obtain their medications through a government program or through private insurance (with a co-pay) are not eligible. Those who pay 100% of the cost of their medicines or who "pay a percentage of the cost (such as 20 percent)" can join. Visit www.thebody.com.

Dirty needles...

…used in health care settings in the developing world contribute to HIV transmission. U.S. researchers reported that needles may have led to more transmissions in Africa than previously realized. The report in the *International Journal of STD & AIDS* referred to studies estimating that as many as 40% of infections in African countries are due to unsterile health care practices. A high level of infections in pregnant women was a red flag, as they may have more access to health care than others do. Also, outbreaks in several poor countries were found to be related to unsterile needles, such as 400 children infected in Libya in 1998.

Viramune in South Africa

Spokespersons for the South African government say it is finally willing to distribute the HIV drug Viramune (nevirapine) to HIV-positive pregnant women attending public health clinics. The government was forced into its decision after losing legal battles against HIV treatment advocates. Viramune by itself successfully prevents perinatal transmission, with just four doses around the time of birth.

Live and Let Live

That was the slogan for World AIDS Day, December 1, 2002. According to the United Nations Programme on AIDS (UNAIDS) World AIDS Campaign, "Live and Let Live is the slogan of the two-year World AIDS Campaign 2002–2003, which will focus on eliminating stigma and discrimination. Stigma and discrimination are the major obstacles to effective HIV/AIDS prevention and care. Fear of discrimination may prevent people from seeking treatment for AIDS or from acknowledging their HIV status publicly. People with, or suspected of having, HIV may be turned away from health care services, denied housing and employment, shunned by their friends and colleagues, turned down for insurance coverage or refused entry into foreign countries. In some cases, they may be evicted from home by their families, divorced by their spouses, and suffer physical violence or even murder. The stigma attached to HIV/AIDS may extend into the next generation, placing an emotional burden on children who may also be trying to cope with the death of their parents from AIDS. With its focus on stigma and discrimination, the campaign will encourage people to break the silence and the barriers to effective HIV/AIDS prevention and care. Only by confronting stigma and discrimination will the fight against HIV/AIDS be won." For materials, visit http://www.unaids.org/wac/2002/index_en.html.

Jim Pickett speaks

Although Jim Pickett mouths off in every issue of *Positively Aware*, readers might appreciate the chance to get to know him a little better through an interview conducted by a student at the Art Institute of Chicago. As you will see—again, Pickett is a passionate, articulate advocate. The photos, however, do not do him justice, and the video clip is a little "scary." Visit www.sperryart.com/jim-pickett.html.

New hep C drug

Pegasys (pegylated interferon) has been FDA approved for treatment of hepatitis C, both by itself and in combination with a new FDA approved ribavirin, Copegus. The combination works about as well as the current standard of care for hepatitis C virus (HCV), a pegylated interferon and ribavirin from another company, Intron A and Rebetol (sold together as Rebetron). But the real story, treatment advocates say, is in the pricing.

Martin Delaney of Project Inform (HIV service organization in San Francisco) and the Fair Pricing Coalition (national) and Brian Klein of the Hepatitis C Action and Advocacy Coalition (national) wrote, "Please note the attached community letter that will be sent to Hoffman-La Roche regarding the excessive price they had set for their new and improved version of interferon called Pegasys. Pegasys alone will cost nearly $14,000 for a year's treatment. In addition, it must be used in combination with an antiviral drug, ribavirin. Currently, ribavirin must be purchased separately from Schering-Plough [or now with Copegus] at a cost of an additional $14,000 to $21,000 (depending on dosage). Thus, the total cost of one year's treatment for HCV, using Pegasys plus ribavirin, would range from $28,000 to $35,000 wholesale (figures are approximate)… .

"At these prices, the great majority of people in need of treatment for HCV will be unable to access it. For those who have only HCV without HIV, there are no such things as ADAP and Ryan White funding, and it is unclear whether Medicaid will be able to put the drug on the formulary for reimbursement. For those with both HCV and HIV, the price all but makes it impossible to cover the drug under the ADAP program or Ryan White funded programs."

In the letter to the head of Roche, advocates say, "We are writing to express our extreme dismay at the pricing actions taken by Hoffmann-La Roche in the launch of its new product, Pegasys, for treatment of HCV infection.

"Several of our members spent a great deal of time and effort attempting to convince your firm that it had an important opportunity in the launch of Pegasys to undercut the outrageous pricing set by Schering for its version of pegylated interferon. We talked about how much easier it would be to establish reimbursement for Pegasys if the price were substantially lower. We hoped to see a price that would make it possible to put the drug on formularies for Medicaid, MediCal and perhaps even the AIDS Drug Assistance Programs (ADAPs), as well as to secure similar forms of reimbursement for HCV patients who are not co-infected with HIV. We stressed how the bulk of the target markets for HCV treatment are not covered by private insurance. We pointed out how high drug prices are forcing people out of the market for private insurance and causing dramatic increases in the "co-pays" for prescription drugs. Earlier on, many advisory board members, activists and HCV coalition members worked with the FDA to clear the path for regulatory approval of Pegasys, stressing the need for competition because of the incredible price charged by Schering. Most of all, we warned Hoffmann-La Roche not to use the Schering price as a standard of reference, but rather make its pricing decision on a higher moral and ethical plane.

"To our dismay, it appears that Hoffman-La Roche wasn't listening. Your company chose a price that, unbelievably, is in fact higher on an annual basis than Schering's: $13,963 for a year's treatment with Pegasys, versus $13,116 for Peg Intron. We have all experienced this as betrayal.

"…Pegasys isn't even a new drug, but rather the application of a well-known modification to an existing drug. It is hard for us to understand how such excess can be ethically justified. We recognize that Pegasys requires a greater quantity of base interferon as a raw material, but certainly not so much that it justifies the incredible annual price.

"We also made a major point that your pricing for Pegasys would be closely watched as an indicator of your intentions with regard to the pricing of the upcoming HIV entry inhibitor Fuzeon… In light of the Pegasys pricing, the company's protestations about the extreme costs of manufacturing Fuzeon will now fall on deaf ears. In its pricing of Pegasys, Hoffmann-La Roche has demonstrated that its pricing policies are based on greed and opportunism rather than legitimate need."

For the entire copy of the letter, visit www.tpan.com.

Moving Forward in HIV Medicine

by Jonathan Uy, MD

Changes in antiretroviral therapy from 2002 to 2003 are more evolutionary than revolutionary. While there are several new agents, including a new drug target, and new formulations of old drugs, what we generally have is consolidation of information that we already know about antiretroviral therapy.

The good news is the developed world has experienced impressive declines in both the incidence of AIDS cases and HIV-related morbidity and mortality.

Once again, the state of antiretroviral therapy is a combination of "good news" and "bad news." The good news is familiar to all who are involved in the treatment of HIV: since the introduction of protease inhibitors in 1995, the developed world has experienced impressive declines in both the incidence of AIDS cases and HIV-related morbidity and mortality. This is primarily due to the use of highly-active antiretroviral therapy (HAART) that can restore and protect immune system function and prevent persons with HIV from progressing to AIDS or dying from an HIV-related condition.

The bad news is also nothing new. Complete viral eradication ("cure") is likely to be impossible, necessitating lifelong antiretroviral therapy, and while many presume that antiretroviral therapy can be effective for years, the long-term durability of HAART has not been established. An extremely high degree of adherence to therapy, higher than has been demanded for any other chronic illness, is also necessary for optimal success. For those who are able to adhere to HAART, medication toxicities and the normal health issues of increasing age, some of which are synergistic, are beginning to be of equal or greater importance than the HIV-specific issues. For those who cannot or will not adhere to HAART, the impact of drug-resistance, which in HIV is likely to be lifelong, can severely limit treatment options.

While there have been comparisons between HIV and other chronic diseases like diabetes mellitus or hypertension, there remain several key differences. No other chronic disease requires such high adherence of potentially toxic drugs, with lack of near-perfect adherence leading to permanent drug resistance. For example, 75% adherence of atenolol does not lead to the permanent loss of the entire beta-blocker class of drugs for treating hypertension! Also, unlike with hypertension and diabetes, we do not know the long-term risks and toxicities of therapy as most of the current antiretroviral drugs have been used for less than a decade. Studying these long-term issues is difficult, especially as new drugs (with new toxicities) continue to be introduced into the mix and practice patterns continue to evolve.

So while the euphoria from antiretroviral therapy's success has been tempered by what we have learned since the mid-1990s, we are hardly back to the pre-HAART era. Thousands are alive and living productive lives today because of HAART, and the science has not stood still. Advances in antiretroviral therapy and our knowledge of HIV continue to move forward and benefit all categories of persons with HIV.

For all persons on antiretroviral therapy, we clearly have a much better understanding of the importance of adherence now than we did in 1996. This is translating to better patient preparation before the initiation of HAART and more ongoing support for better adherence to antiretroviral drugs after HAART is started. This preparation and support is absolutely crucial for maximizing the chances for HAART being successful because of the stringent demands of taking antiretroviral drugs.

The push towards simpler and more tolerable regimens is due in part to this understanding of the importance of adherence. When patients are told that they have to take at least 95% of their medications, even the most minor side effect can become a big deal. Regimens with fewer pills and those given once daily are a significant improvement for many patients. Trizivir at a total of two pills each day continues to be a viable alternative for those with lower pre-treatment viral loads. At the time of this writing, five antiretroviral drugs from all three classes are FDA-approved for once-daily use (amprenavir, didanosine EC, efavirenz, lamivudine, and tenofovir), and there is evidence for the once-daily use of six other antiretroviral drugs either in current or pending formulations (abacavir, atazanavir, lopinavir, nevirapine, saquinavir, and stavudine). While the nature of many once-daily

regimens, particularly ones that include an NNRTI, mean that they usually cannot be used in deep salvage, it is conceivable that a sequence of at least two once-daily regimens can be constructed for antiretroviral-naïve patients.

For deep salvage therapy, the first fusion inhibitor, T-20, brings us a new drug target and with that an antiretroviral drug that should be active against multi-drug resistant virus. While it is only a single agent that, like other antiretroviral drugs, must be combined with other agents to prevent the emergence of drug resistance, it is an option for some who are desperate for additional options.

While there will continue to be newer agents that are simpler to take, better tolerated, and effective against resistant virus, the viral dynamics of HIV make chronic control of the virus by antiretroviral medications an ongoing uphill fight. There may come a day where ever more potent and well-tolerated medications can be given several times a week (like TB therapy), weekly (like pegylated interferon for hepatitis C), or even less frequently with a much greater "forgiveness factor" than current drugs when it comes to missing doses and timing. This would be a clear improvement from our current state.

However, in the minds of many HIV researchers and clinicians, the elusive long-term goal remains a therapeutic vaccine: a treatment that can stimulate one's own immune system to control or suppress HIV long-term rather than eradicating the virus, much as herpes simplex and varicella-zoster (the virus that causes chickenpox and shingles) are usually held in check by an intact immune system but never completely "cured." A therapeutic vaccine would also have life-changing impact in places like sub-Saharan Africa where millions without access to antiretroviral drugs are dying.

Until such time that immune-based therapy is available, we will continue to push on with what we currently have at our disposal. Often lost in the discussion of HIV therapeutics is the message of prevention. HIV infection remains highly preventable, and the advances in therapy should not lessen the message of prevention. As the recent experience in Uganda illustrates, a push towards prevention can be effective even where HAART is not widely available.

As for therapeutics, we will continue to learn how to better use the drugs that we have. Questions such as when to start therapy, how best to sequence therapy, and whether to employ strategies such as treatment interruption in specific populations will continue to be answered, albeit often not perfectly, as prospective trials are completed and retrospective cohorts continue to accumulate data.

More importantly, we have learned that many of these questions are without a definitive answer. The best answer for now is a highly individualized approach. Physicians and patients can sit down together to formulate a customized treatment plan. They can compare current medical knowledge with the unique preferences, desires, hopes, and fears of the patient.

The bad news is complete viral eradication is likely to be impossible. An extremely high degree of adherence to therapy is also necessary for optimal success.

The areas where medical knowledge leaves us with gaps in information need not be filled arbitrarily, but rather give providers the opportunity to discuss these uncertainties with the individual person. And this is something that modern medicine, for all its technology and promise, should be doing anyway.

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What's on the Horizon?

by Charles A. Nelson

It seems that when people try to describe the scope of the HIV/AIDS pandemic, the same words are used year after year—overwhelming, unimaginable and horrific. Sometimes these words lose their power to express how totally devastating living within the AIDS crisis is for many positive individuals. Nonetheless, it is still important for people living with HIV and thier advocates both here and abroad, to get a handle on what is happening, and to monitor the direction of HIV in order to curb this pandemic.

The toll of the pandemic is staggering. HIV claimed more than 3 million lives worldwide in the year 2002 alone. Estimates are that over 40 million people are living with the virus worldwide. In the U.S., an estimated 470,000 deaths have been attributed to HIV/AIDS. In addition, the U.S. has nearly one million HIV-infected individuals, and about 40,000 were infected this year.

In 2002, new advances were made in understanding the new antiretroviral agents, strategies for initiating highly active anti-retrovirial therapy (HAART), and designing effective salvage regimens. However, much remains to be done, as HIV spreads in many parts of the world. In 2002, HIV research and prevention funding is being confronted with its greatest challenge—bioterrorism. Since the anthrax shut-down of the postal system, the National Institutes of Health (NIH) has been pushed to focus more attention on bioterrorism and small pox vaccine development.

As we strive to build on the progress of 2001, many of us face overwhelming stigma and discrimination often associated with HIV infection. Unlike many people afflicted with chronic disease, HIV infected individuals in the U.S. and throughout the world frequently face prejudice and even physical violence because they have the misfortune of being infected with a virus. While most cities in the U.S. have made progress, being shunned by friends, co-workers and even family is still a common experience shared by many HIV positive individuals.

Super HIV Infection

For the first time, a study, by U.S. scientists, has shown that it is possible for an individual to become infected with two closely related strains of HIV. The discovery that the immune system was encountering two markedly different viruses has stunned Harvard's research team. The new case involved a patient whose HIV infection was stable for months during a Structured Treatment Interruption (STI). The implications of super-infection on individual with established HIVAIDS is not yet clear.

There is little doubt that the new data mean changes for all counseling, testing and prevention guidelines to emphasize the risk of transmitting resistant virus between HIV infected individuals. These findings also point out the challenges vaccine developers face in creating a broad, effective vaccine against HIV. It is imperative that safer sex be practiced during each sexual encounter, even if both partners are HIV-infected.

Additional studies are needed to confirm that the super infection seen resulted from infection by a second HIV strain, and to understand why STI stopped working for this individual.

New Treatment Strategies

A strategy of stopping HIV therapies, a few years ago, would have been considered flying in the face of pain-staking gains made since the discovery. As concern about long-term toxicity, metabolic changes, fat redistribution and global drug access increased, therapy interruption strategies were broadly discussed within the activist and scientific communities.

In 2000 at Durban, Fauci kicked off the STI debate when he presented some interesting data and theories about why stopping treatment for controlled periods of time might be beneficial.

People in Fauci's small study saw their viral load spike significantly and then return to undetectable levels once treatment was restarted. With each subsequent interruption, the virus rebounded to a new lower set point. The desired goal of STI strategy is to stimulate the body to produce enough HIV specific key defense cells to maintain the lower viral load with further drug intervention.

HIV targets specific immune cells designed to fight it. A recent study found that those immune cells are three to five times more likely to be infected than other cells designed to attack other diseases. Periodically stopping HIV drug therapy offers a rest period for the body to recover from cumulative side effects, and drug interactions. Structured Treatment

Interruption protocols test a central theory behind this unique treatment plan. In STIs, anti-HIV drugs are usually stopped after the immune system has had to adapt to the virus. STIs appear to work best for individuals who do not have extensive history with HIV drug therapy. Several promising strategies are currently being evaluated but none are ready for broad use by patients.

Most of the activists have recognized that resistance, poor adherence, and side effects to the approved drug would be greatly improved with co-formulation and reduce food restrictions and their dosing schedule. Patients in the ritonavir-boosted arm of the study experienced higher triglycerides and cholesterol levels than the nelfinavir group.

In individuals who have prior PI-experience, doctors are currently considering the use of two PIs boosted with ritonavir. Pharmacokinetic (PK) studies suggest that Kaletra combined with amprenavir requires careful monitoring and dosage adjustment. Increased doses of Kaletra or ritonavir may be required with this combination. Kaletra has shown promising results in reducing viral loads in PI experienced patients combined with amprenavir boosted by ritonavir. Interactions between Kaletra and saquinavir or indinavir still need to be worked out. Available choices for combinations in this salvage setting will depend upon prior treatment history of the patient and results of genotype and phenotype evaluations.

It is imperative that safer sex be practiced during each sexual encounter, even if both partners are HIV-infected.

exploiting our knowledge in boosting current therapies. T-20, FTC, atazanavir and tipranavir, pending arrival on the HIV market, will expand the treatment options for many HIV infected patients and will finally offer patients co-infected with HIV and hepatitis B viable options. The newer versions of older drugs hold promise to lower the total pill burden and improve adherence and bioavailability.

Boosting PIs

Abbott's landmark 863 study launched a new era for PI-based regimens. The study compared Kaletra (which is lopinavir boosted with ritonavir) with unboosted nelfinavir on a backbone of d4T/3TC. Patients in the Kaletra group achieved a higher-level viral load reduction when compared to the nelfinavir group. Since the report of this data several companies have explored the benefits of their drug booted by ritonavir. Patients who have benefited from exploiting drug interactions have been able to reduce pill burden, increase plasma PI concentration,

Opportunistic Infections in the HAART Era

Several reports over the past year show that opportunistic infections (OI) continue to occur both in North America and abroad. Many of these HIV-related complications are due to patients not receiving HAART because of a lack of knowledge that they are infected with HIV, lack of access to care, or failure to achieve adequate suppression of HIV. At the 2002 ICAAC conference, a French study reported that HIV- associated OI deaths and deaths related to other AIDS-related complications ranged between 20–27% during 2000. CMV disease, PCP, tuberculosis, toxoplamosis, atypical mycobacteria and progressive multifocal leukoencephalopathy were the leading causes of HIV-related OI deaths. OIs continue to be a serious burden on the quality of life for many positive people. Patients who appear to have poor access to care are the most likely to bear the burden.

Patients with PCP often stop therapy because of severe drug toxicity or due to the lack of an effective regimen. Between 1989 and 2002, scientists based in Denmark found that 185 of 251 patients had to switch their initial anti-PCP therapy. As HAART became the gold standard for treating HIV, dramatic reductions were seen in the incidence of many OIs in the U.S.

In 2002, HIV research has made substantial progress in important treatment strategies for HIV infection as well as hepatitis B/HIV co-infections. We have gained a better understanding of new antiretrovirals like FTC, atazanavir, T-20 and tipranavir along with their potential drug interactions. Further studies are warranted to design effective strategies for patients in a salvage setting.

Charles A. Nelson, former Director of Treatment Education for NAPWA (National Association of People with AIDS), is a treatment activist who resides in Washington, D.C.

Brand Name: Retrovir

Common Name: zidovudine, AZT

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One 300 mg tablet twice a day (two 100 mg capsules three times a day also available), no food restrictions (with or without food). Clear, strawberry-flavored liquid available for pediatric use. Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: GlaxoSmithKline, www.treathiv.com, 1 (800) 722–9294
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Headaches, fever, chills, muscle soreness, fatigue, nausea, and fingernail discoloration. AZT has been associated with alteration of various cells in the blood through bone marrow suppression resulting in anemia (low red blood cells) and/or neutropenia (low white blood counts), particularly in people with advanced HIV during the first three months. Potential for severe anemia requiring blood transfusion or hospitalization when used on its own or in combination with hydroxyurea. Prolonged use of high doses of AZT has been associated with symptomatic myopathy (muscle damage). Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back) and lactic acidosis (an inability of your body to regulate its acid and bases). This is seen in all patients but is more likely to be severe in women, especially with obesity; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing or shortness of breath); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).
Potential drug interactions: Biaxin (clarithromycin), Mycobutin (rifabutin), and rifampin (under various brand names, used for treating tuberculosis) may decrease AZT blood levels. Benemid (probenecid) may increase AZT blood levels and decrease AZT clearance. Methadone and ganciclovir (Cytovene and Vitrasert) increase AZT blood levels. Prescriber may need to adjust doses accordingly. AZT and Zerit (d4T) shouldn't be used together due to evidence that one limits the other's effectiveness in the test tube. Also, risk of bone marrow toxicity may increase with use of ganciclovir, amphotericin B, pentamidine (NebuPent, Pentam or Pentacarmat), dapsone, flucytosine, interferon-alpha ribavirin (Rebetol), and with other antineoplastics (anti-tumor treatment) such as hydroxyurea. Ribavirin and AZT may cancel each other out, therefore combination use should be avoided.
Tips: Taking with food may minimize upset stomach. Do not use with Hydrea or Droxia (hydroxyurea). Retrovir has somewhat of a bad rep left over from its early years when the doses given were too high. Studies show that Retrovir crosses the blood-brain barrier to a useful degree, which may treat or prevent neurologic damage (such as dementia). Proven to significantly reduce mother-to-infant transmission. Also available in Combivir (one tablet twice a day, combined with Epivir) and in a triple combination in Trizivir (one tablet twice a day combined with both Epivir and Ziagen).
Eight month follow up data was presented at ICAAC 2003 evaluating once a day HAART in treatment naïve patients randomized to a once a day regimen (ddI+3TC+Sustiva, arm A), to a low pill burden twice a day (BID) regimen (AZT+3TC+Sustiva, B) or to a high pill burden BID regimen (AZT+3TC+Viramune, C). There were 32 individuals in each arm. Preliminary results indicate that arm A and B were equal in reducing viral load (81 and 79 %) to undetectable and increasing CD4 T-cell counts; while arm C had the less favorable performance (50%).

Doctor

AZT was the first FDA-approved antiretroviral drug. The patent for AZT expires in 2005. Despite the lack of a significant impact on morbidity and mortality, it was used at that time by many patients as a single agent because there were no other alternatives. Without other agents with which to combine it, doses were often pushed much higher than the current dosage of 300 mg twice daily, leading many taking AZT to experience significant nausea and vomiting. At current doses, this occurs much less frequently, though another potential side effect of AZT, suppression of blood cells (myelosuppression), remains. Resistance to AZT often means resistance to other drugs in this class. Because it has a similar mechanism of action as Zerit (d4T), these drugs should not be given together. For greater simplicity, AZT is often taken as Combivir (AZT and 3TC in one pill) or Trizivir (AZT, 3TC, and abacavir in one pill). —Jonathan Uy, MD

Activist

Retrovir (best known as AZT) is the first drug approved for the treatment of AIDS. This drug has taught the manufacturer, scientist and activist the importance of finding the most effective dose to suppress the HIV virus with minimal side effects. Initially, AZT was approved for treating HIV disease at a dose of 1200–1500 mg a day. Further studies have shown that a lower dose, ranging from 500–600 mg a day, was better tolerated and achieved similar suppression of the HIV virus than the approved higher and more toxic dosage. The majority of people taking this drug experience side effects that resolve over time. AZT continues to serve as a cornerstone of HIV regimens mainly due to its synergistic effect with Epivir (3TC). Since AZT is the grandfather of HIV drugs approved in the USA, patients who are beginning therapy should take a resistance test because approximately 10% of patients may have acquired a virus that is resistant to AZT. —Charles A. Nelson

Potential side effects and toxicity: Peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet, indicating nerve damage that may be reversible but can be painful and permanently debilitating if not treated in time), upset stomach (nausea and vomiting), diarrhea, headache, and more rarely pancreatitis. Other important toxicities include eye changes and optic neuritis. Have periodic eye exam by someone who is aware you are HIV-positive. Increased uric acid levels (indicating a number of disorders, including kidney damage and metabolic diseases), and insomnia are other potential side effects. People with a history of peripheral neuropathy, pancreatitis and heavy alcohol use should avoid Videx EC and Videx. Pancreatitis can be life-threatening and is indicated by increased amylase and lipase levels in lab reports and pain in the stomach and back, along with nausea, vomiting and blood in the urine—risk increases with higher doses, advanced HIV, and alcohol use. Rare but potentially fatal toxicity with all NRTIs: lactic acidosis (an inability of your body to regulate its acid and bases). This is seen in all patients but is more likely to be severe in women, especially with obesity; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing or shortness of breath); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).

Potential drug interactions: Much higher blood levels of Videx are seen in persons who also take Viread (tenofovir) but why this happens is not entirely clear. Doses of Videx may need to be lowered if the medications are taken at the same time of day. The dose of Videx may need increasing when taken with methadone (which lowers Videx blood levels by 41%). Videx/Hivid combination is not recommended because of its higher incidence of peripheral neuropathy. Antineoplastics (antitumor treatment) such as AZT and hydroxyurea may increase risk of peripheral neuropathy. Combining Videx EC/Videx with Zerit with or with hydroxyurea, alcohol, Cytovene, or NebuPent may increase risk of pancreatitis. Also, Cytovene substantually increases Videx levels. Should not be taken within two hours of any prescription antibiotic containing tetracycline. Videx tablets should be taken on an empty stomach two hours apart from protease inhibitors, Tagamet, Nizoral, Sporanox and dapsone, and one hour apart from Rescriptor, while Videx EC can be taken with them (still on an empty stomach).

Tips: Study indicates Videx EC (compared to Videx) may have lower risk of peripheral neuropathy. Swallow the capsules whole (don't break open). Capsules eliminate awful texture of the tablets and the enteric coating reduces diarrhea. Absorption can be decreased by as much as 50 percent when taken with food. Antacids containing magnesium or aluminum may cause adverse side effects if given concurrently with Videx tablets. If you have kidney dysfunction, you may require dose adjustment. Notify your doctor immediately if peripheral neuropathy is suspected, but do not stop taking medication unless directed to do so by your healthcare provider. Take Videx (buffered tablets) on an empty stomach 30 minutes before or two hours after food or drink, except water.

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)

Standard dose: One 400 mg eneteric coated (Videx EC) capsule once a day, with adjustments for weight (two 200 mg capsules also available). Older formulation Videx two 100 mg buffered tablets twice a day (or four tablets once daily). Also, there is powder for oral solution. Take Videx EC strictly on an empty stomach. Take missed dose as soon as possible, but do not double dose.

Manufacturer Contact: Bristol-Myers Squibb, www.bmsvirology.com, 1 (800) 272–4878

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Videx & Videx EC

Common Name: didanosine, ddI

Doctor

There have been several formulations of ddI, and most have been difficult to tolerate due to gastrointestinal side effects. However, the EC formulation of ddI has proven to be much better tolerated. Because it has a different pathway to resistance to the most commonly used drugs in this class (AZT, d4T, 3TC), it often retains potency in patients who have taken many other antiretroviral drugs. The once-daily dosing of Videx EC and its better tolerability also make it a viable component of a once-daily regimen, even in antiretroviral-naïve patients. ddI has a greater association with lipodystrophy and peripheral neuropathy compared with other drugs in this class, but the exact causes of these complications remain unknown. ddI has been given in the past with hydroxyurea, a chemotherapeutic agent used to increase the potency of ddI, but this practice has fallen out of favor because of the side effects of hydroxyurea and the (relative) plethora of other options. —Jonathan Uy, MD

Activist

Videx (the original yucky horse tablet formulation) is the second drug approved for use in combination with other nukes. Early data showed a synergy when take in combination with hydroxurea and d4T. It is critical to take both formulations on an empty stomach. The stomach acidity lowers the amount of the drug that is able to enter the body. Thankfully, the Videx EC (enteric coated) version virtually nullifies the diarrhea commonly associated with the horse tablets. It is still unclear if the lower dosing regimen and/or the new formulation will reduce the common discoloration of the finger nail beds of African Americans. Patients using this drug should discuss signs and potential symptoms of pancreatitis and peripheral neuropathy with their provider before starting this drug. Both formulations have drug interactions with many commonly used prescription medications, most notably with methadone. —Charles A. Nelson

Brand Name: Hivid

Common Name: zalcitabine, ddC

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)
Standard dose: One 0.75 mg tablet three times a day, no food restrictions (with or without food). Liquid available through compassionate use program. Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: Roche Pharmaceuticals, www.rocheusa.com, 1 (800) 282–7780
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet, indicating nerve damage that is reversible but can be painful and permanently debilitating if not treated in time), headache, fever, skin eruptions, canker sores, general inflamation of the mouth, nausea, pancreatitis, malaise (general ill-feeling, as with the blahs, fatigue or a flu). Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back) and lactic acidosis (an inability of your body to regulate its acid and bases). This is seen in all patients but is more likely to be severe in women, especially with obesity; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing or shortness of breath); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).
Potential drug interactions: Due to increased risks associated with peripheral neuropathy, according to the U.S. Department of Health and Human Services (HHS) HIV guidelines, whenever possible Hivid should not be taken with Epivir, Videx or Zerit, Fungizone (amphotericin B), Chloromycetin (chloramphenicol), dapsone, Antabuse (disulfiram), Foscavir (foscarnet), isoniazid (for treating tuberculosis), Dilantin (phenytoin) and Benemid (probenecid). Hivid should not be taken at the same time with magnesium/aluminum containing antacids—decreases Hivid levels by 25%. When used concurrently with Tagamet (cimetidine) and Benemid (probenecid) monitor for renal toxicity. Maalox and Foscavir may decrease Hivid levels. When used with Hivid, pentamidine (NebuPent, Pentam or Pentacarinat, used for treating Pneumocystis *carinii pneumonia*, that is, PCP), may increase risk of pancreatitis, inflammation of the pancreas that can be life-threatening. Pancreatitis is indicated by increased amylase and lipase levels in lab reports and pain in the stomach and back, along with nausea, vomiting and blood in the urine. However, increased amylase levels may not occur until after pancreatitis does. The risk of pancreatitis increases with higher doses, more advanced HIV, and alcohol use. If you experience these symptoms, stop taking Hivid and seek medical attention immediately. If symptoms go away after stopping Hivid, you can consider starting Hivid again at a smaller dose.
Tips: Dual use of Hivid and Videx is not recommended because of the association with a high incidence of peripheral neuropathy. Notify your doctor immediately if peripheral neuropathy is suspected, but do not stop medication unless directed to do so by your healthcare provider.

Doctor

ddC was the third FDA-approved antiretroviral drug. It is now the least-utilized nucleoside reverse transcriptase inhibitor because it is less potent than AZT or ddI, has a similar resistance profile as ddI, and has a similar toxicity profile as ddI. It is also given three-times daily whereas all other drugs in this class are given either once-daily or twice-daily. In an era of simpler regimens in recognition of the central importance of drug adherence, this dosing schedule further relegates ddC as a drug only of historical note. —Jonathan Uy, MD

Activist

ddC is the nuke that lost its niche. When considering the role that ddC may play in your HIV armamentarium, understand that its marginal performance makes it a poor candidate for first or second line regimens. If you are at a stage in your private drug war where your fifth treatment strategy has failed and you're ready to throw the kitchen sink at your HIV virus, ddC may hold some promise. However, few clinical investigators have shown interest in evaluating this drug in recent years. In the desperate days when the HIV treatment guidelines were popular reading and when dual therapy was the treatment strategy of the day, ddC was in high demand despite its less than fabulous data. —Charles A. Nelson

Potential side effects and toxicity: Peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet, indicating nerve damage that can be reversible but could become permanent if not treated in time and that may be debilitating and painful), headache, chills/fever, malaise (overall ill feeling, as with fatigue or a flu), insomnia, anxiety, depression, rash, upset stomach (nausea and vomiting), diarrhea, abdominal pain. Lipodystophy ("buffalo hump"), limb (arm and leg) fat loss (lipoatrophy), and central fat accumulation has been associated with Zerit as well as other antiretrovirals. Rarely, a nerve disorder called transverse descending myelitis can develop (gradual loss of feeling moving from back to feet along the spinal cord). Symptoms may persist after stopping the drug. If symptoms go away after stopping Zerit, you can consider starting Zerit again at a smaller dose. Caregivers of young children should be instructed regarding noticing and reporting peripheral neuropathy. Adverse reactions and serious laboratory abnormalities in children were similar in type and frequency to those seen in adults. Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back) and lactic acidosis (an inability of your body to regulate its acid and bases). This is seen in all patients but is more likely to be severe in women, especially with obesity; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing or shortness of breath); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).

Potential drug interactions: Drugs such as Fungizone (amphotericin B), Foscavir (foscarnet), and dapsone may increase the risk of developing peripheral neuropathy. Cytovene and Vitrasert (ganciclovir) and intravenous Pentam (pentamidine) may increase the risk of pancreatitis. To be used with caution by people with pre-existing bone marrow suppression, renal insufficiency or peripheral neuropathy. AZT and Zerit should not be used together due to evidence that one limits the other's effectiveness in the test tube. Because of additive neurotoxicity, if possible, stavudine should not be combined with zalcitabine (Hivid).

Tips: Contact your doctor immediately if peripheral neuropathy is suspected, but do not stop taking medication unless directed to do so by your healthcare provider. Stop taking Zerit immediately if experiencing symptoms of pancreatitis: pain in the stomach that sometimes extends to the chest and the back, along with nausea, vomiting or blood in the urine. Get immediate medical attention. Increased amylase levels indicate pancreatitis, but sometimes levels do not increase until after pancreatitis occurs. Studies show that Zerit crosses the blood-brain barrier to a useful degree, which may treat or prevent neurological damage (such as dementia).

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)

Standard dose: One 40 mg capsule twice a day for people weighing 132 pounds (60 kg) or more, or one 30 mg capsule twice a day for people weighing less; no food restrictions. Available in 15 mg, 20 mg, 30 mg and 40 mg capsules; check for food restrictions. Also powder for oral solution. Take missed dose as soon as possible, but do not double dose.

Manufacturer Contact: Bristol-Myers Squibb, www.bmsvirology.com, 1 (800) 272–4878

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Zerit

Common Name: stavudine, d4T

Doctor

d4T was the fourth FDA-approved antiretroviral drug. While it has a similar mechanism of action and similar resistance profile to AZT, some studies in the pre-HAART era showed good d4T activity in patients with AZT experience. Advantages of d4T over AZT include the lack of myelosuppression, making d4T a good choice in patients with anemia. d4T is also very well-tolerated without the gastrointestinal side effects associated with AZT. However, d4T does have a greater association with lipodystrophy and peripheral neuropathy compared with other drugs in this class, but the exact causes of these complications remain unknown. A once-daily formulation of d4T has been submitted to the FDA for approval, which is expected to come soon. Resistance to d4T usually means resistance to other drugs in this class. Because it has a similar mechanism of action as AZT, these drugs should not be given together. —Jonathan Uy, MD

Activist

Zerit's rapid development was delayed because its sister nuke (ddI) was further along the FDA approval path despite the vocal objections from activists. For patients and physicians, d4T has been a popular choice as one leg of an antiviral regimen for many years. Early studies found that d4T was as effective as AZT and was shown to be less toxic. There is a growing body of data linking d4T to loss of body fat (lipoatrophy) and liver toxicity with or without a potentially fatal build up of acid in the body, known as lactic acidosis. Patients using this drug should discuss signs and potential symptoms of pancreatitis and lactic acidosis with their provider before starting this drug. Be on the safe side and have your liver enzymes monitored frequently while taking the product. One comment from the 2002 reviewer of d4T bears repeating …"It is important to choose the dosage of d4T according to body weight: less than 132 lbs: 30 mg, greater than 132 lbs: 40 mg." —Charles A. Nelson

Positively Aware
The Journal of Test Positive Aware Network

2003 HIV Drug Chart

#Not actual size

*Each drug is recommended for use in combination with other antiretrovirals. Dose may be adjusted when taken in combination.

Drug Class	Brand (Generic Name)	Adult Single Dose#	Adult Regimen*	Food and liquid qualifications
Protease Inhibitors (PI)	Agenerase (amprenavir)		Eight 150-mg capsules, twice daily	May be taken with or without food, but a high fat meal decreases absorption and should be avoided.
	Crixivan (indinavir)		Two 400-mg capsules, every 8 hours	Take one hour before or two hours after meal with water
	Fortovase (saquinavir soft-gel)		Six 200-mg capsules, three times a day—must be taken with Norvir	Take with meal or within two hours after a meal
	Invirase (saquinavir hard-gel)		Three 200 mg hard-gel capsules three times a day	Take with food, or within two hours after a meal
	Kaletra (lopinavir/ritonavir)		Three capsules (133.3-mg lopinavir/33.3-mg ritonavir), twice daily	Take with food
	Norvir (ritonavir)		Six 100-mg capsules, twice daily (start with 300-mg twice daily and increase by 100-mg twice daily every 2-3 days)	Take with food, if possible
	Viracept (nelfinavir)		Three 250-mg tablets three times a day (or five 250-mg tablets, twice daily)	Take with a meal or light snack
Nucleoside Reverse Transcriptase Inhibitor (NRTI)	Combivir (lamivudine/zidovudine)		One tablet (150-mg lamivudine, 300-mg zidovudine), twice daily	No food restrictions
	Epivir (lamivudine, 3TC)		One 300-mg tablet, once daily or one 150-mg tablet, twice daily	No food restrictions
	Hivid (zalcitabine, ddC)		One 0.75-mg tablet, three times a day	No food restrictions
	Retrovir (zidovudine, AZT)		One 300-mg tablet, twice daily	No food restrictions
	Trizivir (abacavir/lamivudine/ zidovudine)		One tablet (300-mg abacavir, 150-mg lamivudine, 300-mg zidovudine), twice daily	No food restrictions
	Videx EC (didanosine, ddI)		One 400-mg capsule daily for adults weighing 132lbs/60kg or more	Take on an empty stomach, at least 30 minutes before or 2 hours after a meal
	Zerit (stavudine, d4T)		One 40-mg capsule, twice daily for adults weighing 132lbs/60kg or more	No food restrictions
	Ziagen (abacavir sulfate)		One 300-mg tablet, twice daily	No food restrictions
Nucleotide (NRTI)	Viread (tenofovir)		One 300-mg tablet daily	Take with food
Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI)	Rescriptor (delavirdine)		Two 200-mg tablets, three times a day	No food restrictions (take one hour apart from antacids)
	Sustiva (efavirenz)		One 600-mg tablet daily	Avoid taking with high fat meal
	Viramune (nevirapine)		One 200-mg tablet daily for the first 14 days, then one 200-mg tablet, twice daily	No food restrictions

Brand Name: Epivir

Common Name: lamivudine, 3TC

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)
Standard dose: One 300 mg tablet once a day (or two 150 mg tablets once a day), with no food restrictions (may be taken with or without food). May be taken as one 150 mg tablet twice a day. Dose needs to be lowered for people who weigh less than 110 pounds (50 kg), to 2 mg/kg (a kilogram equals 2.2 pounds).
Strawberry/banana flavored liquid available. Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: GlaxoSmithKline, www.treathiv.com, 1 (800) 722–9294
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: One of the most easily tolerated medications. Headache, nausea, diarrhea, fatigue, hair loss, insomnia, malaise (overall ill feeling, as with the blahs, fatigue or a flu), nasal symptoms, cough, peripheral neuropathy, low white blood cells and anemia. In early studies in children, in higher doses than now used we saw pancreatitis, a potentially fatal condition. Children should be monitored carefully for this condition. Symptoms include nausea, vomiting, clammy skin, and stomach pain that often extends to the back, along with increased amylase in the blood. Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back) and lactic acidosis (an inability of your body to regulate its acid and bases). This is seen in all patients but is more likely to be severe in women, especially with obesity; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing or shortness of breath); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).
Potential drug interactions: No significant interactions.
Tips: Is also approved for treatment of hepatitis B virus (HBV), under the brand name Epivir HBV and used at a different dose, as is Viread (tenofovir). However drug resistance usually develops after prolonged monotherapy. Whereas Epivir has shown to be effective in eliminating HBV in co-infected HIV/HBV individuals, data presented at the 14th International AIDS Conference 2002 indicates the use of Epivir in patients without HIV infection only rarely leads to clearance of HBV infection. Furthermore, the once-daily dose for HBV may cause drug resistance (it may no longer work) for people with HIV. Epivir is also available combined with Retrovir (Combivir, one tablet twice a day) and in a triple combination with both Retrovir and Ziagen (Trizivir, one tablet twice a day).

Doctor

While it is associated with NRTI class toxicities like every other NRTI, 3TC is the single best-tolerated antiretroviral drug with minimal side effects. Its tolerability and potency (for a NRTI) make it the ideal antiretroviral drug, but it needs to be combined with other less-than-perfect drugs to form a HAART regimen. Frequently used as part of a first HAART regimen, 3TC is often the first drug against which the virus shows resistance when a regimen fails because it has a low genetic barrier to drug resistance. Different than all the other drugs in the NRTI class, a single mutation at RT position 184 confers high-level 3TC resistance. This mutation does not by itself confer resistance against other NRTI's and actually makes the virus hypersuceptible to AZT, d4T, and tenofovir, illustrating the complexity of interpreting genotypic resistance tests. In 2002, 3TC in its current formulation was FDA-approved for once-daily use. —Jonathan Uy, MD

Activist

3TC has become a widely used antiviral in combination with non-nukes and protease inhibitors, partly due to its pill size, low toxicity and limited side effect profile. It is most commonly given in combination with AZT or d4T and less often with ddI. One drawback to this drug is that resistance to 3TC emerges quickly when doses are missed. The take over of Burroughs Wellcome by Glaxo Pharmaceuticals facilitated the co-formulation of 3TC and AZT into one pill (Combivir). Now we have the triple threat of 3TC, AZT, and abacavir known as Trizivir. 3TC also has been shown to control the hepatitis B virus even if there is HIV resistance. Early reports have implied a beneficial effect between 3TC and Viread (tenofovir). Larger studies will be needed to confirm any suspected synergy. —Charles A. Nelson

Potential side effects and toxicity: Hypersensitivity (allergic reaction, HSR) to Ziagen can be fatal. People who think they are experiencing hypersensitivity must be evaluated by an experienced HIV provider as soon as possible before they stop taking Ziagen. If they are indeed having the HSR, they cannot take it again (called "rechallenging"), because of life-threatening and in a few instances fatal reaction. Hypersensitivity usually occurs within two weeks of starting therapy, gets progressively worse and resolves quickly (24–48 hours) after permanent discontinuation. Approximately 5% of people taking Ziagen experienced hypersensitivity during clinical trials. There are a number of primary symptoms of HSR, but the most important fact is combinations of symptoms. These usually, but not always include some combination of low-grade fever with muscle ache, severe nausea, vomiting or other gastrointestinal upset (including abdominal pain), malaise (run-down feeling, as with the blahs, fatigue or a flu), respiratory symptoms (cough, difficulty breathing and sore throat) and possibly mild rash. Hypersensitivity might be confused with flu during flu season. The manufacturer recommends that people with symptoms of acute respiratory disease consider hypersensitivity even if other diagnosis such as pneumonia, bronchitis or flu is possible. If hypersensitivity is suspected, stop therapy and contact your doctor immediately. There should be no problem with this if you miss your doses for a few days and did not have an allergic reaction. Black box warning strengthened in 2001 when hypersensitivity wasn't recognized and people went back on Ziagen, becoming seriously ill, so tell your doctor if you have ever taken this before!
Other potential side effects include nausea, vomiting, diarrhea, fatigue, headache, fever, rash, anorexia (loss of appetite), high blood sugar and high triglyceride levels (fat in the blood). Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back) and lactic acidosis (an inability of your body to regulate its acid and bases). This is seen in all patients but is more likely to be severe in women, especially with obesity; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing or shortness of breath); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side).
Potential drug interactions: Avoid concommitant alcohol ingestion. Alcohol increases Ziagen levels and might increase its side effects. No clinically significant interactions between Ziagen and other drugs have been observed. This did not increase the risk for HSR.
Tips: Ziagen has the potential to cross the blood-brain barrier, which may prevent or treat neurological damage (such as dementia). The pattern of viral resistance to abacavir is similar to that of other NRTIs, though abacavir can retain some activity when other NRTI's have lost most activity.

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI, or nuke)
Standard dose: One 300 mg tablet twice a day, no food restrictions (may be taken with or without food). Strawberry/banana flavored liquid available. Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: GlaxoSmithKline, www.ziagen.com, 1 (800) 722–9294
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Ziagen

Common Name: abacavir sulfate

Doctor

Abacavir initially showed promise as an NRTI with the potency of a PI with a 1.8 log viral load decline at 4 weeks when given as monotherapy. With this strategy in mind, Trizivir, a combination of abacavir, AZT, and 3TC in one pill, allows for a simplified regimen of one pill twice daily. Unfortunately, this regimen has not been as effective at higher pre-treatment viral loads, limiting its practical usefulness. The other issue that has significantly limited the utilization of abacavir is a severe allergic reaction (hypersensitivity) that occurs in about 5% of patients. The greater danger lies in re-starting abacavir after it has been stopped due to hypersensitivity, as this can result in death. Recently, researchers have discovered a genetic predisposition to abacavir hypersensitivity, but testing for this gene (HLA B27) is not routinely done because the lack of this gene does not guarantee that one will not have hypersensitivity.
—Jonathan Uy, MD

Activist

The super nuke with a potent and potentially deadly punch. The manufacturer has promoted this drug to be a cornerstone in HAART and an alternative to a PI based regimen. While the HIV clinical guidelines do not recommend Ziagen as a first line therapy, for patients with limited HIV drug experience, abacavir is potent, tolerable, and convenient, but its role in an HIV treatment regimen is still unclear. It does not seem to be as effective for treatment-experienced patients who have become resistant to many approved nukes and PIs. On the downside, a serious life-threatening allergic reaction is seen in reportedly 5% of patients. However in a recent report from the ZORRO observational cohort study, serious adverse events occurred in 4 of the 128 volunteers subjects, and 10 experienced a suspected abacavir allergic reaction. This report pushes the allergic reaction count closer to 11%. —Charles A. Nelson

Brand Name: Combivir

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One tablet (150 mg lamivudine, 300 mg zidovudine), twice a day, with no food restrictions (may be taken with or without food). Take with food to decrease AZT associated nausea if it happens. Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: GlaxoSmithKline, www.combivir.com, 1 (800) 722–9294
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: See Retrovir/zidovudine (AZT) and Epivir/lamivudine (3TC).
Potential drug interactions: See Retrovir/zidovudine (AZT) and Epivir/lamivudine (3TC).
Tips: Combivir is the combination of Retrovir/zidovudine (AZT) and Epivir/lamivudine (3TC) into one pill; see the pages of those individual drugs for more information.

Doctor

See comments on Retrovir (AZT) and Epivir (3TC).
—Jonathan Uy, MD

Activist

Simply, this product is the result of the corporate merger fever that was common a few years ago. With multiple studies reporting benefits from regimens containing a nuke backbone of these two products, Glaxo decided to take over Burroughs Wellcome to create the beginnings of a super HIV pill. Kudos to Glaxo on leading the corporate field in co-formulation of HIV drugs. For many years now, treatment activists have argued with the pharmaceutical industry that co-formulation eases challenges to adherence and reduces the pill burden that many of us endure every day. Glaxo's solution to the problem of how to protect two companies' confidential data and pricing information is a slightly different take on the community's request for companies to work together and share data in our common fight to end this pandemic. —Charles A. Nelson

Potential side effects and toxicity: See Retrovir/zidovudine (AZT), Epivir/lamivudine (3TC) and Ziagen (abacavir).
Potential drug interactions: See hypersensitivity warning on Ziagen (abacavir), also see Retrovir/zidovudine (AZT), Epivir/lamivudine (3TC).
Tips: Trizivir has proven to be a popular triple-nuke regimen among providers and for many individuals using HIV drugs for the first time and with a low-to-moderate viral load. Trizivir, the triple-nuke combo, saves the other classes of drugs for later if necessary. An abstract (WePeB5829) presented at the 14th International AIDS Conference 2002, showed that Trizivir (triple nuke regimen) had good results in decreasing viral load and increasing CD4 T-cells in treatment experienced, non-adherence patients (84% of 50 total study participants had IDU experience). Participants entered the study with viral loads greater than 5000 copies/mL. There still continues to be limited data on the use of this triple-combo regimen in people with viral loads greater then 100,000 copies/mL. New information on resistance and cumulative exposure to nukes should be considered as well before starting this regimen.
Trizivir is the combination of Retrovir/zidovudine (AZT), Epivir/lamivudine (3TC) and Ziagen (abacavir) into one pill; see the pages of those individual drugs for more information.

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One tablet (300 mg abacavir, 150 mg lamivudine, 300 mg zidovudine), twice a day, no food restrictions (may be taken with or without food). Take with food to decrease AZT associated nausea if it happens. Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: GlaxoSmithKline, www.treathiv.com, 1 (800) 722–9294
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Trizivir

Doctor

See comments on Retrovir (AZT), Epivir (3TC), and Ziagen (abacavir). —Jonathan Uy, MD

Activist

GlaxoSmithKline's marketing of this product appears to moving HIV drug therapy to a single pill taken twice a day. If GSK can overcome the seemingly increasing allergic reaction data then patients starting HIV therapy will have a clear choice. Brilliant marketing I must say. Perhaps the community should intensify discussions with GSK on expanding their international clinical research and drug donation program. As with Combivir, people should be aware that Trizivir is a combination of three drugs (AZT + 3TC + abacavir) and so increases the possibility of side effects and drug interactions. It also muddies the waters in determining with which drug a patient may be experiencing problems. For treatment-experienced patients our search for a "super drug combination" continues. For them, there is little need to seriously consider Trizivir as a viable treatment option. The data just ain't pointing in that direction. —Charles A. Nelson

Brand Name: Coviracil

Common Name: emtricitabine, FTC

Photo not available because of experimental drug status.

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Experimental dose: Not yet established because of experiemental drug status. In Phase III trials dose has been one 200 mg capsule once a day.
Manufacturer Contact: Triangle Pharmaceuticals, Inc. and Gilead Sciences 1 (800) 455–3235
AIDS Clinical Trials Information Service: 1 (800) TRIALS–A (874–2572)
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Currently in Phase III of development.
Tips: Coviracil (FTC) is expected to be approved for anti-HIV therapy in 2003. Sometimes called a "me-too" drug because of its similarity to Epivir (3TC); both are associated with the M184V mutation (which suggests drug resistance). Coviracil has demonstrated efficacy against HBV/HIV *in vitro* (in a test tube). In one ICAAC 2002 presentation (abstract H-2050), FTC and 3TC demonstrated similar results. Study participants with incomplete suppression of viral load (greater than 50 copies/mL) had an increased risk of virologic failure compared to patients with complete viral suppression (less than 50 copies/mL). In those participants with the presence of M184V mutation at study entry there was a greater occurrence of virologic failure. Most recently, in a large, advanced (Phase III) clinical trial, the Data Safety Monitoring Board (an independent committee of experts that review and oversee studies) recommended that the trial be unblinded and all participants offered Coviracil (FTC). It was statistically superior in safety and efficacy over Zerit (d4T). The two drugs were given in blinded fashion (neither participants nor clinic staff knew which drug was being given) in combination with Videx and Sustiva (although it is already known that combining Zerit and Videx increases the risk for side effects associated with each medicine); results from this study were also presented at ICAAC 2002 (late breaker abstract LB-1). A total of 571 (285 d4T arm, 286 FTC arm) participants were enrolled. The median baseline viral load was 4.9 log and the median baseline CD4 T-cell count was 288 cells for both arms of the study.

Doctor

FTC is an NRTI that is similar in structure to 3TC and has yet to receive FDA approval. It appears to be more potent than 3TC, and has always been slated to be given once-daily. However, as 3TC itself is now approved for once-daily administration, that aspect of FTC is now not as compelling. Drug resistance to FTC and 3TC are also similar, so if the virus is resistant to 3TC, it will also be resistant to FTC. Given that 3TC is often included in a first HAART regimen and is often the first drug against which drug resistance develops, and that 3TC is a well-known and well-tolerated agent that can now be given once-daily, it remains to be seen whether there will be a large demand for FTC even with its increased potency. The FDA is apparently thinking along the same lines. It is also unknown whether and how the pending purchase of Triangle Pharmaceuticals (makers of FTC) by Gilead Sciences will affect the approval of FTC.
—Jonathan Uy, MD

Activist

Gilead has followed the spree of mergers to expand their drug line with its recent acquisition of Triangle. This acquisition solves a lot of problems faced by Gilead, manufacturer of Viread (tenofovir DF), and positions them to combine the two drugs (Viread and FTC) into a single pill. This co-formulation would improve adherence and expand the treatment options to treat HIV and hepatitis B. The combination of Coviracil (FTC) and Viread (tenofovir DF) would offer these patients a once-a-day treatment option. FTC could gain FDA approval by Fall 2003 but a hepatitis B indication may take longer to receive. Triangle has two other mid-stage clinical trials currently active, one for AIDS and one for hepatitis B. —Charles A. Nelson

Potential side effects and toxicity: Overall, fairly well tolerated, but limited experience with this agent abounds. Long-term data still being analyzed, however, can experience the following: nausea, headache, diarrhea, vomiting, asthenia, flatulence, abdominal pain and anorexia. Rare but potentially fatal toxicity with all NRTIs: pancreatitis (signs include nausea, vomiting, and abdominal pain that often spreads to the chest and back) and lactic acidosis (an inability of your body to regulate its acid and bases). This is seen in all patients but is more likely to be severe in women, especially with obesity; greater risk for people with underlying liver disease; signs include deep muscle fatigue, especially in legs, and difficulty breathing or shortness of breath); and enlarged, fatty liver (called hepatomegaly with steatosis; check for tenderness below ribs on right side). The effect of tenofovir on children and individuals with severe hepatic impairment was not studied during drug development. However, since tenofovir is not metabolized by the liver (and appears to have less toxicity in the liver than the majority of the NRTIs) it is believed the impact on individuals with liver disease should be minimal.

Potential drug interactions: The FDA recently issued an advisory on the co-administration of Viread and Videx EC or Videx tablets (ddI). Videx EC and Videx tablets (ddI) have increased levels when given at the same time as Viread (tenofovir). The exact amount of dose reduction needed in Videx when given with Viread is not known, but many clinicians are using the 250 mg Videx EC with Viread, so as to maintain the once daily dosing regimens. There is no clinical data to show this is going to be better or worse at this time.

Tips: Unlike the nucleosides, nucleotides can enter uninfected cells, and once there, protect against infection. To its credit, Viread is successful in showing viral load decrease in people with nuke resistance and continues to demonstrate good results in the growing number of people whose current triple-class therapy is failing. Epivir resistance seems to reverse Viread resistance, however the jury is still out on the clinical significance of this one. Also, just because it's in a new drug class doesn't mean it can't have cross resistance to other nukes. Viread may have cross-resistance with other HIV medicines, exactly which ones are still being determined, but no new mutations were seen with its use in clinical trials. In clinical trials reduced responses to Viread were associated with multiple TAMs (thymidine analog mutations) including the M41L or L210W. Less toxicity in the liver than the majority of NRTIs. The body clears 70–80% of the drug through the kidneys, so dose adjustment in kidney dysfunction is needed. So far, serious kidney problems have been rare. The manufacturer recommends that individuals with impaired renal (eye) function not use Viread.

Like Epivir HBV, tenofovir has activity against hepatitis B. While data is limited, it appears that tenofovir can have prolonged activity against hepatitis B even when resistant to 3TC.

Class: nucleotide analog (also called nucleotide reverse transcriptase inhibitor—part of the nucleosides—NRTI, or nuke)
Standard dose: One 300 mg tablet once a day, take with food. Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: Gilead Sciences, Inc., www.viread.com, 1 (800) 455–3235
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Viread

Common Name: tenofovir disoproxil fumarate

Doctor

Tenofovir is the first nucleotide reverse transcriptase inhibitor FDA-approved to treat HIV. Tenofovir also appears to have much less renal toxicity than adefovir (at HIV doses), and it is generally well-tolerated. Its simple pill burden and dosage schedule (one pill once daily) make it an attractive drug, in both antiretroviral-naïve and experienced patients. A recent study has shown it to be equivalent to d4T as part of a HAART regimen in antiretroviral-naïve patients. While tenofovir does have activity against drug-resistant virus, making it a good candidate for salvage therapy, extensive NRTI-resistance does limit its potency. It is also unclear how antiretroviral-naïve HIV develops resistance against tenofovir. —Jonathan Uy, MD

Activist

After a long and rocky road, Gilead has hit a home run with Viread (tenofovir DF). Viread is a nucleotide with excellent activity against HIV as well as HBV. Its activity against HBV shows that it is well tolerated and can achieve significant viral reduction of both viruses. A Viread containing regimen may be a more attractive option for co-infected patients. Adding the alternative treatment for HBV (adefovir) would complicate any treatment plan and increase risk of significant drug interactions. Also taking low dose adefovir may promote HIV mutations and further limit treatment options available to patients. In treatment-experienced patients, Viread achieved a 0.6 log reduction in viral load. When compared with the 1.5 log reduction gained in treatment naïve patients, it appears that Viread may not be extremely helpful in a salvage setting. However, I'll take any reduction if I were in that setting. —Charles A. Nelson

Brand Name: Rescriptor

Common Name: delavirdine

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)
Standard dose: Two 200 mg tablets three times a day (or four 100 mg tablets three times a day; can be dissolved in liquid [avoid grapefruit juice]), no food restrictions (may be taken with or without food). Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: Agouron Pharmaceuticals, www.agouron.com, 1 (888) 777–6637
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Rash, headache, upset stomach (nausea and vomiting), diarrhea, fatigue and pruritus (itchy skin), elevated liver enzymes. Severe rash observed in NNRTI class can be life-threatening. Signs may include fever, blistering, oral lesions, conjunctivitis (pink eye, which if untreated may result in permanent loss of vision), swelling, muscle or joint aches, or general malaise (feeling unwell, as with a flu). Stop taking Rescriptor if these symptoms appear and seek immediate medical attention.
Potential drug interactions: Do not use Zocor (simvastatin) or Mevacor (lovastatin) lipid lowering agents; suggested alternatives are Lipitor (atorvastatin), Lescol (fluvastatin), and Pravachol (pravastatin, the one that looks best on paper for people on protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Versed (midazolam) and Xanax (alprazolam) should not be used concurrently with Rescriptor. Potential toxicity when given with Biaxin (clarithromycin), dapsone, Mycobutin (rifabutin), ergot derivatives (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams), Procardia (nitedipine), Coumadin (warfarin) and quinidine. Tegretol (carbamazepine, an anti-seizure medication used to treat peripheral neuropathy), phenobarbital, Dilantin (phenytoin), Mycobutin (rifabutin) and rifampin (under various brand names, used to treat tuberculosis) are drugs that decrease Rescriptor levels. Certain amphetamines and antiarrhythmic drugs should not be used with Rescriptor. Use of Tagamet (cimetedine) and other drugs in that class is not recommended because they may reduce the absorption of Rescriptor. Rescriptor increases Crixivan, Fortovase, Invirase, Kaletra and atazanavir levels. Absorption of Rescriptor is decreased with antacids, including Videx (because of its antacid buffer), so take at least one hour apart from these drugs. Prescriber may need to adjust doses of all these drugs accordingly.
Tips: Research demonstrates Rescriptor ability to increase blood levels of protease inhibitors. This makes it unique among the NNRTIs. The doses needed with the protease inhibitors and Rescriptor is not clear, but may be considered an option in someone who has significant cardiac risk factors and the provider does not want to worry about additionally elevating blood fats. Antacids and gastric achlorhydria (low stomach acid) decreases absorption. Take one hour before or after antacids and with acidic beverages such as orange or cranberry juice for achlorhydria. The drug level is increased 20% when the 100 mg tablets are given as a slurry (disintegrating drug in water; drink the rinse as well).

Doctor

Delavirdine was the second FDA-approved non-nucleoside reverse transcriptase inhibitor, a class of antiretroviral drug that has become an alternative to protease inhibitors. It is the least-used NNRTI, partly because of its three-times daily administration. Like other NNRTIs, some patients can develop a hypersensitivity reaction to delavirdine which can include a rash and fever; most do not have to stop the medication. Resistance to all NNRTIs, including delavirdine, is usually conferred by the same single amino acid substitutions. As a result, most patients have only one shot at using this class. —Jonathan Uy, MD

Activist

Recent reports show that delavirdine increases plasma drug concentrations for the majority of approved PI class, namely indinavir, nelfinavir, ritonavir, amprenavir and saquinavir plasma levels. It is not clear how this interesting interaction data will be utilized. Are we to see a future co-formulated nelfinavir-delavirdine twice-a-day pill soon? Can delavirdine share the stage with ritonavir in the role as a booster drug? Careful attention should be used when considering an NNRTI booster. Early data shows that resistance to delavirdine can develop rather fast and leading to resistance to the entire class of NNRTIs. Can taking low doses of delavirdine reduce the many side effects common to a PI-containing regimen? Will resistance to the entire class of NNRTIs increase based on treatment strategies utilizing low dose delavirdine to boost existing drug therapy, or reduce mother to child transmission, as has been a proposed use for nevirapine? Is this a fair trade off? —Charles A. Nelson

Potential side effects and toxicity: Rash, headache, and stomach (nausea and vomiting). An increase in liver enzyme levels has been observed, in rare instances the development of hepatitis occurs as frequently with this drug as the other non-nukes. May need to stop taking nevirapine until liver function returns to normal. Permanently discontinue if abnormalities return. Although rare, severe and life-threatening skin reactions and hepatotoxicity (liver damage), including fatal cases of each, have occurred. The reason for the 14-day lead-in dosing is to reduce the frequency of rash. Symptoms of severe rash may include fever, blistering, oral lesions, conjunctivitis (pink eye, which if untreated may result in permanent loss of vision), swelling, muscle or joint aches, or general malaise (feeling unwell, as with a flu). If these symptoms are observed stop taking Viramune and seek immediate medical attention. Do not increase dose if rash develops during dose escalation or if you develop any rash accompanied by the above listed conditions. Small studies found that 40–50 mg prednisone during induction period can lessen the risk. (People with hypertension or diabetes were not allowed to take prednisone.) Granulocytopenia (the loss of a specific type of white blood cell) is more common in children than in adults.

Potential drug interactions: May cause methadone withdrawal. Viramune reduces levels of protease inhibitors and they should not be taken at the same time or the doses must be increased. Crixivan should be increased to 1,000 mg every eight hours. Kaletra should be increased to four capsules twice a day. Viramune interacts with rifampin requiring dose adjustment, but none with Mycobutin (rifabutin). The effectiveness of birth control pills may be decreased when taking Viramune; women and their partners should consider the use of alternative contraception methods with barrier.

Tips: Because of the high incidence of rash associated with Viramune, examine yourself thoroughly for the slightest sign of rash. Notify your doctor of any rash, even mild. Rash may be avoided by using dose escalation schedule. One analysis found more rash, and more severe rash, in women. Use of pretreatment, such as prednisone or Benadryl (diphenhydramine), a non-prescription oral antihistamine, may be used to minimize the risk of rash and to control itching but the reaction can actually be worse—discuss it with your doctor. A topical (placed on the skin) hydrocortisone or an oatmeal-containing cream, such as Aveeno, may improve comfort. Topical antihistamine-containing products should be avoided since there have been reports of irritation and rashes spreading. Monitor liver function tests during first six months.

Studies suggest that Viramune crosses the blood-brain barrier to a useful degree; when given around the time time of labor Viramune has demonstrated effectiveness in preventing the transmission of HIV from mother to child, but there was an increase in resistance.

Recently, nevirapine has been shown to positively effect cholesterol and triglycerides in patients, so the manufacturer is conducting research to further define the magnitude of this.

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI, or non-nuke)

Standard dose: One 200 mg tablet daily for two weeks, then full dose of one 200 mg twice daily from then on. If rash occurs in first two weeks, it is important to report condition to physician as soon as possible. No food restrictions (with or without food). Liquid formulation is available. Take missed dose as soon as possible, but do not double dose.

Manufacturer Contact: Boehringer-Ingelheim, www.viramune.com, 1 (800) 274–8651

AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Viramune

Common Name: nevirapine

Doctor

Nevirapine was the first FDA-approved NNRTI. Like all other current NNRTIs, resistance to nevirapine develops rapidly when given as monotherapy. This is demonstrated by the appearance of nevirapine resistance after a single dose of nevirapine given to women to prevent vertical transmission in developing countries. Also, as with the other NNRTIs, some patients can develop a hypersensitivity reaction when starting nevirapine. For this reason, nevirapine is usually given at half of the usual dose for the first two weeks. Nevirapine does not have to be discontinued for most mild to moderate hypersensitivity reactions. Unique to nevirapine is the development of hepatitis, at times severe, also usually during the first several weeks of treatment. Nevirapine is labeled for twice-daily administration, but pharmacokinetic and clinical data support its once-daily use. —Jonathan Uy, MD

Activist

Nevirapine is a relatively inexpensive drug with an expanding role in the global HIV pandemic. It has shown remarkable ability to reduce HIV viral transmission when women take it close to delivery. This drug reduces the absorption of several HIV meds and, like all NNRTIs, resistance can develop quickly if not taken properly. Nevirapine can also be hard for the liver to process the drug out of your body. Monitoring your liver functions is wise. All three manufacturers of the approved NNRTIs should explore ways to determine who will and who will not develop the potentially life threatening rash reaction. As discussions on global drug access and explorations of alternative treatment interruption strategies continue, understanding the risk of increased NNRTI resistance in addition to understanding the biologic predictors of this serious rash reaction are needed, given the high percentage of people experiencing this reaction from the entire NNRTI class. —Charles A. Nelson

Brand Name: Sustiva

Common Name: efavirenz

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)
Standard dose: One 600 mg tablet, typically at bedtime; no food restrictions (with or without food, but avoid high fat meals). Also available in smaller 50 mg, 100 mg and 200 mg capsules. Dose can be split up. Approved for children three years and older. Strawberry/mint flavored solution available to children under expanded access program. Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: Bristol-Myers Squibb, www.sustiva.com; 1 (800) 334–4486
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: About 50% of patients experience some kind of central nervous system (CNS) symptoms (dizziness, headache, somnolence or hypnotic trance), psychiatric symptoms (confusion, insomnia, hallucinations, vivid dreams or nightmares, depression, euphoria or mania, agitation), rash, upset stomach (nausea and vomiting), diarrhea, fever, insomnia and increased liver enzymes. These symptoms occur early and generally resolve within two to four weeks. In a small number of patients, including those with substance use experience, serious psychiatric symptoms have been reported. Some people in recovery from substance use experience flashbacks. May lead to false positive tests for use of marijuana (see Editor's Note). Rash is the most common adverse event (about 1/3 of patients). Rash is more common, and more severe, in children, as is diarrhea, fever and low levels of neutrophils. Women taking Sustiva should not become pregnant or breast feed because of the risk of birth defects.
Potential drug interactions: May cause methadone withdrawal. When taken with Sustiva, Crixivan should be increased to 1,000 mg every eight hours. Kaletra should be increased to four capsules twice a day. Sustiva and saquinavir (Fortovase and Invirase) should not be used in combination, because levels of Fortovase are decreased substantially. No interaction data available with Fortovase/Norvir—consider doubling Fortovase to 800 mg twice a day. Sustiva and Norvir increase when used together and may increase risk of liver damage and other potential side effects. Do not take with Versed (midazolam), Halcion (triazolam), or ergot medications (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams). Do not use with Biaxin (clarithromyocin), as levels of Biaxin are reduced. May affect Coumadin (warfarin) therapy. Back-up birth control method to the Pill is recommended because of potential for embryo heart defects.
Tips: It is recommended that Sustiva be taken at bedtime to help reduce CNS symptoms (seen in half of all adults taking it), but can be taken at any time. Avoid driving or operating heavy machinery for a few hours after dose. Side effects may linger. Some people can handle Sustiva better when taking Ativan or Ambien to sleep for the first few weeks, but both of these may make you even more groggy the next day. High-fat food as well as alcohol may increase the concentration of Sustiva and the risk of experiencing side effects.
Strong results with Combivir (slightly better than Crixivan/Combivir) and follow-up data showing equivalence to all current protease regimens (including Kaletra and atazanavir) led to making Sustiva the first drug that's not a protease inhibitor to be added to US guidelines for first-line HIV therapy. Recently shown to penetrate lymphoid tissue, an HIV hiding place. Slightly raises levels of triglycerides and the good cholesterol (HDL). Monitor liver enzymes. Antihistamines or corticosteriods can hasten the resolution of rash, but do not take as a precautionary agent. Severe rash can be life-threatening (see Viramune). Corresponding with the CNS side effects, Sustiva penetrates readily into the brain. Children have the same side effects as adults (primarily in the CNS).

Doctor

Efavirenz is the only NNRTI listed as a strongly recommended HAART component by the 2002 DHHS guidelines. It is a very potent antiretroviral drug but has the same issue of hypersensitivity and rapid resistance because of a low genetic barrier to drug resistance as other NNRTIs. The same single amino acid substitutions usually confer resistance to all NNRTIs including efavirenz. Efavirenz is associated with CNS-related side effects including vivid dreams and drowsiness. While these can often resolve after the first several weeks of treatment, many patients continue to have some symptoms indefinitely, but most patients find efavirenz very easy to take in the long-term. Multiple clinical trial results show efavirenz to be as potent as any protease inhibitor, taking into account those who stop treatment due to intolerance. —Jonathan Uy, MD

Activist

Sustiva is the shining star of the NNRTI class. As early promising reports surfaced of Sustiva achieving equivalent suppression of the HIV virus when compared to the 1997 standard of care, which was then Crixivan, AZT and 3TC, interest in this product sky-rocketed. Sustiva offers patients a potent and viable alternative to the common side effects of Crixivan and other PI-based regimens. The drug's biggest misfortune is its impact on the central nervous system. Some 50% of patients taking Sustiva have characterized this side effect as creating an "altered mental state" in which you may experience vivid dreams as well as other neurologic and metabolic side effects. The three 200 mg capsules can be taken throughout the day to lessen the side effects. —Charles A. Nelson

Potential side effects and toxicity: Diarrhea, abdominal discomfort and nausea, few other side effects seen, due to low absorption (4 to 6%). Seen with all older protease inhibitors are increased levels of cholesterol and triglycerides (except Agenerase and possibly atazanavir) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.
Potential drug interactions: Do not use Zocor or Mevacor; lipid-lowering alternatives are Lipitor (atorvastain), Lescol (fluvastatin), and Pravachol (parvastatin), but they should be used with caution due to potential for liver toxicity. Do not take with Seldane, Hismanal (astemizole), Seldane (terfenadine) Halcion (triazolam), Versed (midazolam), Propulsid (cisapride), ergot medications (such as Wigraine and Cafergot, in any form. Viramune and Mycobutin (rifabutin) decreases Invirase levels. Invirase may increase dapsone levels. Antifungal Nizoral (ketoconazole), used for treatment of candidiasis (thrush), triples Invirase's bioavailability from 4 to 15%. Do not take with birth control pills; Invirase reduces level of ethinyl estradiol by 40%. Prescriber may need to adjust doses accordingly. Rescriptor, Crixivan, Norvir and Viracept all significantly increase Invirase's plasma concentrations. Protease inhibitors increase blood levels of Viagra (sidenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction.
Tips: Due to its poor bioavailability and a new formulation (Fortovase), Invirase was used so sparingly that it was even dropped from the pages of this Drug Guide. In fact, if you go to www.invirase.com, you're taken to the Fortovase web page! In Houston last year, for example, pharmacies had no Invirase on their shelves and were waiting for supplies as prescriptions skyrocketed. However, Invirase is back, due to study results indicating strong efficacy with fewer side effects when taken with a mini-dose of Norvir, as compared to Fortovase/Norvir (go figure). This older version of saquinavir hard-gel capsules is rarely used except in combination with Norvir (low-dose) to minimize gastrointestinal adverse events. Patrick Clay advises, "Get the hell out of the doctor's office if you don't get Norvir." Must be taken with food.

Class: HIV protease inhibitor (PI)
Standard dose: Three 200 mg hard-gel capsules three times a day with food, or within two hours after a meal. However, should be dosed in combination with Norvir. Invirase 1600 mg + 100 or 200 mg Norvir once-a-day or Invirase 800 mg + 100 mg Norvir twice-a-day. Take a missed dose as soon as possible, but do not double the next dose.
Manufacturer Contact: Roche Pharmaceuticals, www.rocheusa.com, 1 (800) 910–4687
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Invirase

Common Name: saquinavir hard-gel

Doctor

The original formulation of saquinavir approved for the treatment of HIV-1 infection was saquinavir mesylate (Invirase), followed by the development of a newer soft gelatin capsule (SGC) formulation (Fortovase) in 1997, characterized by substantially improved bioavailability. Invirase absorption with a high-fat meal is poor (4%), whereas that of Fortovase is substantially better. Food increases Fortovase levels, such that drug should be taken within two hours of a meal, unless taken with Norvir. Recent studies have demonstrated greater efficacy with either the SGC formulation or when boosted with Norvir, which causes an ~20-fold increase in saquinavir levels. In one study of treatment-naïve adults, regimens containing either Fortovase or Invirase were compared; at 72 weeks, 57% of Fortovase and 38% of Invirase recipients had viral loads <400 c/ml. —Kristin Lee, MD

Activist

No statement provided.

Brand Name: Crixivan

Common Name: indinavir

Class: HIV protease inhibitor (PI)
Standard dose: Strict schedule of two 400 mg capsules (800 mg) every 8 hours on empty stomach (an hour before or two hours after eating) or with low-fat snack (call for food list). Take a missed dose as soon as possible, but do not double the next dose. 200 mg and 333 mg capsules available.
Manufacturer Contact: Merck and Co., www.crixivan.com, 1 (800) 850–3430
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Headache, nausea and kidney stones, which may lead to more serious problems such as kidney failure. Signs include back pain, fever, abdominal tenderness, and painful urination. Call your doctor immediately if pain develops in the middle to lower stomach or the back, or if there is blood in the urine. Other potential side effects include hair loss, changed skin color, severe skin reactions (such as horribly dry skin), fatigue or weakness, malaise (feeling unwell, as with the blahs, fatigue or a flu), nausea, diarrhea, loss of appetite, ingrown toe nails (often requiring minor surgery), dry mouth, headache, taste changes, and liver toxicity. Increased uric acid indicates kidney damage. Symptoms include joint pain and arthritis. Hemolytic anemia, the premature destruction of red blood cells, is rare but dangerous: watch for unusual fatigue, jaundice (yellowing of eyes and skin), or reddish-brown urine, and monitor red blood cell counts. Watch out for other drugs also associated with this condition (such as Septra and dapsone). Seen with all older protease inhibitors are increased levels of cholesterol and triglycerides (except Agenerase and possibly atazanavir) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.
Potential drug interactions: Viracept increases levels of Crixivan and using 1200 mg of Crixivan with 1250 mg of Viracept twice daily will give the same levels as 800 mg Crixivan every 8 hours (with a light meal). Increase Crixivan to 1,000 mg three times a day when taken with Viramune or Sustiva. Reduce dosage if using Nizoral (600 mg every 8 hours). Do not use Zocor or Mevacor; lipid-lowering alternatives are Lipitor (atorvastain), Lescol (fluvastatin), and Pravachol (parvastatin), but they should be used with caution because of potential for liver toxicity. Do not take with Halcion (triazolam), Versed (midazolam), Propulsid (cisapride), ergot medications (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams). The dose of rifampin (Mycobutin) should be reduced by 50% when using with Crixivan. Protease inhibitors increase blood levels of Viagra (sidenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction.
Tips: Full-dose Crixivan is a rarity these days, but combining with small doses of Norvir is becoming increasingly popular. It avoids food restrictions, can be taken twice a day, at a smaller dose, but drink at least 48 oz fluids daily, preferably water or clear liquids (soda pop doesn't count!). Large amounts of coffee or alcohol can increase risk of stones. Stones may continue after stopping Crixivan. Concurrent ingestion of grapefruit juice decreases Crixivan blood levels. Should be stored in original container and kept dry. Hair loss due to Crixivan is mild and will grow back within 4 months when switched to another PI or NNRTI.

Doctor

Crixivan was the third PI approved by the FDA in 1996. Because it requires an acidic environment for optimal solubility, absorption is improved with fasting or a light meal, or co-administered with Norvir, with a 77% reduction in levels observed with a full meal. As previously noted, trials combining Crixivan with Norvir have demonstrated favorable pharmacokinetics, with substantive increases in Crixivan levels allowing for BID dosing. One study of Norvir intensification in patients with detectable viral loads in Crixivan-containing regimens demonstrated a viral load <50 c/ml in 38% of patients at 48 weeks. The most serious adverse event involving Crixivan is nephrolithiasis, causing symptoms in 4-9% of recipients, typically treated supportively without necessitating treatment interruption. Incidence can be reduced via adequate amounts of fluids (minimum of 1.5 liters/day). —Kristin Lee, MD

Activist

Indinavir holds the position as the "gold standard" on which current HAART therapy is based. Early data was not encouraging on this drug. Many early patients became resistant to indinavir quickly while others showed good early responses that waned over time. Once the correct dosing schedule was finally found, the three-drug combo of AZT/3TC/Indinavir became the first regimen to significantly suppress viral replication below detection. To maximize the benefit from an indinavir containing regimen is dependant on how regimented you are about following a precise dosing schedule of every eight hours. To avoid the common painful kidney stone, it must be taken on an empty stomach and with plenty of water. If you can cope with the demanding every eight-hour schedule, dry cracking skin and the risk of developing an occasional kidney stone, this drug offers a powerful option. —Charles A. Nelson

Potential side effects and toxicity: Asthenia (weakness), abdominal pain, upset stomach (nausea, diarrhea, and vomiting), tingling/numbness around the mouth, hands or feet, loss of appetite, taste disturbance, headache, dizziness, pancreatitis (see nukes), and alcohol intolerance. Seen with all older protease inhibitors are increased levels of cholesterol and triglycerides (except Agenerase and possibly atazanavir) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs. Norvir has been shown to increase liver enzymes (AST, ALT and GGT), muscle enzyme (CPK), and uric acid.

Potential drug interactions: Do not use Zocor or Mevacor; lipid-lowering alternatives are Lipitor (atorvastain), Lescol (fluvastatin), and Pravachol (parvastatin), but they should be used with caution because of potential for liver toxicity. Alternatives should still be used with caution because of potential for liver toxicity. Cannot be taken with Cordarone (amiodarone), ergot derivatives such as Cafergot (in any form—serious interactions seen with dilation during gynecological exams), Migranal, D.H.E. 45, Halcion, Orap, quinidine, Rythmol, Tambocor, Vascor, and Versed. Protease inhibitors increase blood levels of Viagra (sidenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. One report suggested Viagra should start at half that when taken by someone on Norvir. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction. The street drug Ecstasy is greatly increased by Norvir, and at least one death has been attributed to the combination. GHB is also dangerous with Norvir. Tobacco and alcohol may lower blood levels of Norvir. Increases seen in clarithromycin (Biaxin) levels by 80 percent. Rifampin decreases Norvir levels by 35 percent. Contains alcohol (but should not be enough to trigger relapse) and greatly hastens intoxication. Norvir should not be taken with Antabuse or Flagyl.

Tips: Convenient twice-daily dosing with food is offset by high rate of side effects and early drop-out. The real strength of Norvir is in combination with other protease inhibitors (used as a boosting agent), allowing for a lower dose of both. Take with fatty food when combined with Fortovase or Viracept. Taking it right before a meal may help. Taking with food—especially high fat such as peanut butter or avocado—may help prevent stomach upset. Capsules do not need refrigeration if stored below 77° F and used within 30 days. Keep in original container. The capsules contain castor oil and have bitter taste. The liquid tastes foul and activates children's gag reflex. Watch for increased cholesterol and triglyceride levels, especially if heart disease runs in your family. Remember to get fasting levels.

Class: HIV protease inhibitor (PI)
Standard dose: Six 100 mg (600 mg) soft gelatin capsules twice a day, preferably with food. Dose escalation is important to avoid side effects: 3 capsules (300 mg) twice a day for two or three days, then increase dose by one capsule (100 mg) every two or three days until reaching full 600 mg dose. Take a missed dose as soon as possible, but do not double the next dose. Approved for children ages 3 and older. Liquid formula available, but tastes unbelievably horrific.
Manufacturer Contact: Abbott Laboratories, www.norvir.com, 1 (800) 222–6885
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Norvir

Common Name: ritonavir

Doctor

The activity of Norvir has been studied extensively, with more recent studies examining Norvir in combination with other PIs by virtue of its ability to increase most PI concentrations and half-life. A study of boosted saquinavir demonstrated that Norvir/saquinavir/d4T was as effective as Crixivan plus two NRTIs. In addition, recent pharmacokinetic studies have demonstrated a highly favorable impact on Crixivan levels, allowing for simplification to a BID regimen. In addition, Norvir as a single agent is poorly tolerated, with the most frequent reported side effects including GI intolerance and circumoral and peripheral peristhesias. Hepatotoxicity, hypercholesterolemia and triglyceridemia are more frequent with Norvir compared to other PIs, though the risk may be reduced with lower Norvir doses used in boosted PI combinations. Resistance correlates with mutations at codons 46, 63, 71, 82, and 84. —Kristin Lee, MD

Activist

Ritonavir was one of the fastest HIV drugs recommended by the FDA advisory panel. Patients and doctors were very excited about the early data; in broader use found a larger percentage of adverse drug interactions. Ritonavir interferes by increasing or decreasing co-administered medications. The advantage of being a powerful inhibitor is that a small amount of ritonavir goes a long way. Data has shown that ritonavir. It is used mainly as a boosting agent to support other PIs duration of effectiveness. The more common side effect reported is the old friend of most PIs—diarrhea and a unique numbness around the mouth. It is not clear what role ritonavir may play in the fat redistribution challenge faced by many treatment experience patients. In HIV-negative adults, ritonavir increased triglycerides and cholesterol levels. —Charles A. Nelson

Brand Name: Viracept

Common Name: nelfinavir

Class: HIV protease inhibitor (PI)
Standard dose: Three 250 mg tablets three times a day or five 250 mg tablets (1250 mg) twice a day with food. (Two 625 mg tablets twice a day expected someday). Take a missed dose as soon as possible, but do not double the next dose. Viracept Oral Powder also available for children and individuals unable to swallow tablets.
Manufacturer Contact: Agouron Pharamaceuticals, www.viracept.com, 1 (888) 777–6637
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Diarrhea (33% of patients), stomach discomfort, nausea, flatulence (gas), asthenia (weakness), and rash. Seen with all older protease inhibitors are increased levels of cholesterol and triglycerides (except Agenerase and possibly atazanavir) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.
Potential drug interactions: In general, less severe interactions compared to ritonavir, Kaletra, indinavir, saquinavir and amprenavir. The jury is still out on atazanavir—stay posted. Do not use Zocor or Mevacor; lipid-lowering alternatives are Lipitor (atorvastain), Lescol (fluvastatin), and Pravachol (parvastatin), but they should be used with caution because of potential for liver toxicity. Do not take with Halcion (triazolam), Versed (midazolam), Cordarone, quinidine, ergot medications (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams). Blood levels of Viracept are reduced by rifampin and may be reduced by phenobarbital, phenytoin, and carbamazepine (Tegretol and others). Fortovase levels increase three- to five-fold, Crixivan increases 50% (see Crixivan for potential drug interactions) and Norvir levels are unchanged. Prescriber may need to adjust doses of any of these drugs accordingly. Protease inhibitors increase blood levels of Viagra (sidenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction. Mycobutin (rifabutin) dose must be decreased when used with Viracept. Rifampin and Viracept should not be used together. Reduces effectiveness of birth control pills, so use alternative contraceptive with barrier.
Tips: Viracept tablets have a film coating which helps to prevent them from dissolving while swallowing. Do not leave the pharmacy without anti-diarrhea medication available without a prescription, such as Imodium. Take a change of clothes with you when you leave home for the first several weeks—stick it out, most often symptoms improve after two or three weeks. Try Solgar oat bran tablets, psyllium husk fiber bars, calcium supplements (including Tums or Rolaids) and pancreatic enzymes (all with meals). First protease inhibitor choice for children who cannot swallow capsules or tablets, but solution tastes horrible and requires a large amount for mixing into food. It's preferable to crush adult tablets for use in children. Acidic food or juice (e.g. orange/apple juice or apple sauce) not recommended in combination with Viracept, due to resulting bitter taste.
Viracept is mostly a first line protease inhibitor. More likely to be salvaged if resistance develops compared to some other protease inhibitors, however you have to be on the medicine when the resistance test is done for the test to work.

Doctor

Viracept was the fourth PI approved by the FDA, noteworthy for good oral bioavailability, with conconmitant administration of food resulting in 2-to-3-fold increases in plasma concentrations. Development of a simplified regimen involving two pills BID is underway. Studies of dual-PI regimens containing Viracept have not been studied extensively, with the exception of Viracept-saquinavir, which is complicated by a high pill burden. However, one study of patients with extensive NRTI exposure evaluated strategies involving 1-2 new NRTIs plus Viracept, Sustiva, or both, with virologic suppression at <50 c/ml at 48 weeks found in 22%/Viracept, 44%/Sustiva, 67%/Viracept/Sustiva. Diarrhea/loose stools management strategies include oat bran/psyllium, loperamide, and calcium. —Kristin Lee, MD

Activist

Nelfinavir, more than most PIs, is plagued by seemingly unending diarrhea. Agouron should develop self-cleaning skivvies and provide them to patients with prescription refill. It is the least they can do given the many special little nelfinavir perks we find in our whites all too frequently. Despite the bathroom challenges, nelfinavir is a potent and tolerable PI. At least it has increased the bathroom private time for many of us. The film coating has virtually eliminated the most common problem in taking this drug. I still wake up in a cold sweat dreaming about the one nelfinavir capsule becoming stuck and blocking off my airway every day. Try Imodium, Ultrase (a pancreatic enzyme) or other antidiarrhea medications, if you don't want to increase your purchasing power on skivvies. Depending on your genotype test, nelfinavir has been reported to show benefit in salvage therapy setting. —Charles A. Nelson

Potential side effects and toxicity: Diarrhea, nausea, abdominal discomfort or pain, flatulence (gas), indigestion, headaches, insomnia, fatigue, and taste alteration. Seen with all older protease inhibitors are increased levels of cholesterol and triglycerides (except Agenerase and possibly atazanavir) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.

Potential drug interactions: Do not use Zocor or Mevacor lipid-lowering drugs; suggested alternatives are Lipitor, Lescol, and Pravachol (looks best on paper for protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Increased blood levels with Crixivan, Norvir and Viracept. Blood levels decreased significantly by Sustiva, but can be taken together if Norvir is included. Fortovase should not be taken with rifampin or Mycobutin. Other drugs that may also reduce Fortovase blood levels are Decadron and Tegretol, Dilantin, and phenobarbital. Do not take with Halcion, Versed, sedatives/hypnotics, ergot devivatives (such as Wigraine and Cafergot, in any form—serious interactions seen with dilation during gynecological exams), Seldane and Hismanal. High incidence of liver problems, and severe ones, when taken with Rescriptor. Protease inhibitors increase blood levels of Viagra (sildenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction. Mycobutin (rifabutin), phenobarbital, phenytoin dexamethasone and carbamazepine (Tegretol and others), Viramune and Sustiva decrease Fortovase levels (but the last two can be taken if Norvir is added). Rescriptor, Crixivan, Norvir and Viracept all significantly increase Fortovase plasma concentrations, but Crixivan may be antagonistic. The side effects of calcium channel blockers, clindamycin, dapsone and quinidine may be increased if taken with saquinavir.

Tips: Must be taken with food or within two hours after a meal. Keep capsules at room temperature if they will be used up within three months. Zantac, Pepcid, Tagamet or antacids may be necessary to treat Fortovase heartburn (which is common). Refrigerated (36–46° F or 2–8° C) capsules remain stable until the expiration date printed on the label. Once brought to room temperature capsules should be used within 3 months. Avoid direct sunlight. Long popular when taken twice a day with Norvir (ritonavir), both dosed at 400 mg each. Optional lower dosings of Fortovase boosted with Norvir being studied—five 200 mg Fortovase with one 100 mg Norvir twice a day *or* eight 200 mg Fortovase with one 100 mg Norvir once-a-day *or* five 200 mg Fortovase with three 133 mg Kaletra [lopinavir/ritonavir] twice a day, some limited information is favorable.

Class: HIV protease inhibitor (PI)
Standard dose: Six 200 mg soft-gel capsules three times a day with food, or within two hours after a meal. Take missed dose as soon as possible, but do not double dose.
Manfacturer Contact: Roche Pharmaceuticals, www.fortovase.com, 1 (800) 910–4687
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Fortovase

Common Name: saquinavir soft-gel

Doctor

The original formulation of saquinavir approved for the treatment of HIV-1 infection was saquinavir mesylate (Invirase), followed by the development of a newer soft gelatin capsule (SGC) formulation (Fortovase) in 1997, characterized by substantially improved bioavailability. Invirase absorption with a high-fat meal is poor (4%), whereas that of Fortovase is substantially better. Food increases Fortovase levels, such that drug should be taken within two hours of a meal, unless taken with Norvir. Recent studies have demonstrated greater efficacy with either the SGC formulation or when boosted with Norvir, which causes an ~20-fold increase in saquinavir levels. In one study of treatment-naïve adults, regimens containing either Fortovase or Invirase were compared; at 72 weeks, 57% of Fortovase and 38% of Invirase recipients had viral loads <400 c/ml. —Kristin Lee, MD

Activist

Fortovase is the new and improved version of the hard to absorb Invirase. The reformulation would have moved the soft-gel son of saquinavir into the preferred option column if you did not have to gag on 18 pills a day. Combining 400 mg of the soft-gel capsules with 400 mg of ritonavir twice a day has been shown to be effective, plus this regimen reduces the pill count to a manageable number. All PIs can cause metabolic dysfunctions, redistribution of body fat, the onset of diabetes and liver toxicity. Before taking other meds with Fortovase double check with your local pharmacist about possible drug interactions. The hard capsule formulation is still used but rarely as the single PI. When starting this regimen watch out for GI problems. The diarrhea, nausea and gas can be a surprise when they occur all at once. —Charles A. Nelson

Brand Name: Agenerase

Common Name: amprenavir

Class: HIV protease inhibitor (PI)
Standard dose: Eight 150 mg (1200 mg) soft gelatin capsules twice a day, no food restrictions (with or without food, but avoid high fat meals). 50 mg capsule also available. Take missed dose as soon as possible, but do not double dose. Approved for children ages 4 and older. Grape, bubblegum, peppermint flavored liquid available. Adults should not use liquid if possible.
Manufacturer Contact: GlaxoSmithKline, www.treathiv.com, 1 (800) 722–9294
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Rash (20% of patients on study) upset stomach (nausea and vomiting) abdominal pain, taste disorders, fatigue, headache, anemia, colitis, bruising easily, prolonged bleeding, depressive or mood disorders, circumoral paresthesia (tingling or numbing around the mouth) and peripheral paresthesia. Gaseous symptoms are common and may be severe. Taking with food may help, but check for pancreatitis when there is severe stomach pain. Seen with all older protease inhibitors are increased levels of cholesterol and triglycerides (except Agenerase and possibly atazanavir) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.
Potential drug interactions: Do not use Zocor or Mevacor lipid-lowering drugs; suggested alternatives are Lipitor, Lescol, and Pravachol (looks best on paper for protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Rescriptor and Viracept greatly increase Agenerase blood levels (and usually stomach discomfort) and prescriber may need to adjust dose accordingly. Sustiva has been shown to significantly reduce blood levels of Agenerase unless also taken with Norvir mini-dose. Interacts with several antihistamines, sedatives, and anti-fungal drugs. Do not use with rifampin. When Agenerase and Methadone are used in combination, levels of Methadone can decrease. Dose reduction of Mycobutin is necessary. Increased blood levels and drug activity are seen with dapsone, erythromycin, Sporonox, Xanax, Tranxene, Valium, flurazepam, Cardene, Procardia or Adalat CC and Nimotop. Each capsule contains vitamin E, so avoid taking with other blood thinners, such as Coumadin (warfarin), clotting factor, vitamin K, and low-dose daily aspirin, as well as herbs such as ginger, garlic, feverfew, ginseng and gingko biloba. Ibuprofren (Advil) can also be problematic. Do not take extra vitamin E. Protease inhibitors increase blood levels of Viagra (sidenafil citrate), and Viagra dose should be started at 12.5 mg and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction.
Tips: The huge number of pills are a major drawback. Two alternative dosings are being used—eight 150 mg Agenerase with two 100 mg Norvir once-a-day *or* four 150 mg Agenerase with one 100 mg Norvir twice a day. However, Norvir significantly increased cholesterol and triglycerides. May also penetrate the lymph nodes, where virus can hide out. Severe rash can be life-threatening (grade 3 or 4, see Viramune). Avoid taking with food high in fat. Label warning: Agenerase Oral Solution should not be given to infants and children below the age of 4 years. Should not be used by pregnant women, because the larger amount of propylene glycol in this formluation may be harmful to the fetus.

Doctor

Agenerase is well absorbed orally, without food restrictions. Though clinical efficacy has been demonstrated, the pill burden of the current recommended dosage of 1200 mg BID (16 pills/day) has limited tolerability. A multicenter study of primary HIV infection using AZT/3TC/Ziagen/Agenerase demonstrated a viral decrease <50 c/ml in 87% at 28 weeks; utility in heavily PI-experienced patients has not been shown. More recently, trials of Norvir-intensified Agenerase regimens have shown good virologic suppression and improved tolerance. Major side effects include GI intolerance, headache, and circumoral paresthesias. Therapeutic trials have shown high drop-out rates due to adverse reactions, primarily nausea, vomiting, and rash. The 150V mutation is unique to Agenerase and is associated with the highest levels of Agenerase resistance.
—Kristin Lee, MD

Activist

Amprenavir requires patients to take 16 pills a day to achieve an effective blood concentration level. By the time this drug received the FDA's blessing and approval, many patients had exhausted their treatment options due to intolerable side effects, adherence challenges or development of cross-resistant mutations to the available PIs. Don't get your hopes up if you fall within the multiple cross-resistant group. Amprenavir levels are boosted with the addition of 100 mg of ritonavir; this regimen brings the pill count down to four pills twice a day. GSK is working hard on studies of the second generation of amprenavir. The pro-drug formulation will lower the pill count and improve its potency. The leading side effects of amprenavir are diarrhea, gas and nausea particularly when combined with AZT. A mild rash is rare. Patients should note that this formulation contains sulfa, so if you had a reaction to Bactrim, for example, look out for a similar response. —Charles A. Nelson

Potential side effects and toxicity: Rash, loose stools, diarrhea, nausea, headache, muscle weakness, increased cholesterol and triglycerides (fats in the blood), and AST/ALT (liver function tests, a sign of liver damage). These were not fasting samples, that are needed for the most accurate results. Seen with all older protease inhibitors are increased levels of cholesterol and triglycerides (except Agenerase and possibly atazanavir) and perhaps associated heart disease, lipodystrophy (body fat changes, including thinning of the face, arms and legs, with or without fat accumulation in the stomach, breasts and sometimes the upper back), worsening or new cases of diabetes (symptoms include increased thirst and hunger, frequent urination, unexplained weight loss, fatigue, and dry itchy skin; see your doctor promptly) and increased bleeding in hemophiliacs.

Potential drug interactions: Dosage of methadone may need to be increased when taken with Kaletra. Increase Kaletra dose to 4 capsules twice a day with food recommended when using with Sustiva or Viramune in people who previously took HIV drugs, especially protease inhibitors. May lower levels of Retrovir and Ziagen. Do not use Zocor or Mevacor; suggested alternatives are Lipitor, Lescol, and Pravachol (looks best on paper for protease inhibitors). Alternatives should still be used with caution because of potential for liver toxicity. Protease inhibitors increase blood levels of Viagra, and Viagra dose should be started at 12.5 mg (half the normal dose) and increased as needed and tolerated. It's recommended that people do not exceed 25 mg in a 48 hour period because of potential for fatal reaction. Phenobarbital, phenytoin (Dilantin and others) or carbamazepine (Tegretol and others) may lower blood levels of Kaletra. Reduces effectiveness of birth control pills; use alternative contraceptive. Oral solution contains alcohol, so do not use with Antabuse or Flagyl. Do not take with Tambocor (flecainide), Rythmol (propafenone), Hismanol, Seldane, rifampin, ergot derivatives (such as Cafetrate, Cafergot, Wigraine and Methergine, in any form—serious interactions seen with dilation during gynecological exams), D.H.E. 45, St. John's Wort, pimozide, Versed and Halcion. Also dihydropuridine calcium channel blockers. Videx should be given an hour before or two hours after Kaletra, as Kaletra should be taken with food. Rifabutin dose must be lowered.

Tips: Doctors and patients report that this protease inhibitor is very tolerable. Great viral load results out to 96 weeks (significant) in people on their first HIV regimen. Good results also seen in heavily treatment-experienced children and adults, even those with protease inhibitor resistance. However, drug-experienced people also used a non-nuke, which may mean that three classes of HIV drugs are needed for them, and which limits future options. Then again, some people don't have many options. Expected to successfully control HIV that no longer responds to other meds due to drug resistance, but cross-resistance has already been seen. Can have Norvir's yucky taste and taste aversion. Manufacturer is conducting trials examining strength and durability of once-a-day dosing.

Class: HIV protease inhibitor (PI)
Standard dose: Three soft-gelatin capsules (133.3 mg lopinavir and 33.3 mg ritonavir each) twice a day, preferably with food; liquid formula available. Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: Abbott Laboratories, www.kaletra.com, 1 (800) 222–6885
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Brand Name: Kaletra

Common Name: lopinavir/ritonavir

Doctor

Kaletra, the most recently FDA approved PI, takes advantage of the boosting effect of Norvir. Efficacy has been demonstrated in both treatment naïve and salvage regimens. One study of 653 treatment-naïve patients compared lopinavir/Norvir and Viracept, each combined with d4T/3TC; 48-week intent to treat analysis demonstrated viral suppression to <50 c/ml in 67% of lopinavir/Norvir recipients compared with 52% of Viracept recipients. A study of 70 NNRTI-naïve patients with viremia on PI regimens received lopinavir/Norvir + Viramune + 2 NRTIs, of which 60% had a viral load<50 c/ml via intent to treat analysis at 48 weeks. The most common side effect is GI intolerance, with 15-25% of study patients reporting diarrhea of at least moderate severity. —Kristin Lee, MD

Activist

It seems that Abbott has hit a home run with Kaletra. Data show that it is effective in patients who were unable to construct viable treatment options. This potent inhibitor of viral replication is a co-formulation of two drugs—lopinavir and a small amount of ritonavir. Kaletra achieves significant efficacy in combination with efavirenz (Sustiva) for patients with extensive PI experience. The company reports that they have not been able to find patients who have developed resistance to this drug. If you believe that you fall within a unique category—contact the company. A recent analysis of Abbott's extended trial (study 720) of Kaletra/d4T/3TC in patients with limited HIV drug experience revealed that transient blips in viral load (above 50 copies) were not uncommon. The inability to achieve or consistently maintain viral suppression through the 4 years of follow-up is a minor dent in Kaletra's impressive performance. —Charles A. Nelson

Brand Name: Not yet established

Common Name: tipranavir

Photo not available because of experimental drug status.

Class: experimental protease inhibitor
Standard dose: Dose not yet established because of experimental drug status, but studies are going forward with a dose of 500 mg with 200 mg of ritonavir twice a day.
Manufacturer contact: Boehringer-Ingelheim, www.boehringer-ingelheim.com
AIDS Clinical Trials Information Service: 1 (800) TRIALS–A (874–2572)

Potential side effects and toxicity: Gastrointestinal related, mild diarrhea, nausea, vomiting and fatigue. In clinical trials symptoms have been managed by having a light snack with the drug. Fairly well tolerated in Phase II studies, but full side effect profile isn't usually determined until drugs move into Phase III.
Potential drug interactions: Not yet finalized. This drug is metabolized by the liver (same as most of the other protease inhibitors).
Tips: Tipranavir is the first non-peptidic protease inhibitor (NPPI) in development for the treatment of HIV infection (a different chemical structure). Current and future studies designed to determine most optimal dose have been conducted in patients with documented drug resistance to HIV, so kudos to the manufacturer for taking the high road. In studies, very limited cross-resistance has been seen and significant viral load decrease was seen in people with protease inhibitor resistance who took tipranavir by itself (for less than a month). Still, it should not be cross-resistant to other protease inhibitors. Phase III studies are being initiated in early 2003. Look around for these trials, if you have multiple protease inhibitor resistance, they will be targeting you.

Doctor

No statement provided.

Activist

Tipranavir is the first in a unique class of PI currently in a Phase II study of its clinical development. It would have been closer to approval if Pharmacia-UpJohn, the original manufacturer, was more invested in HIV drug development. From the earlier clinical results, the most effective dose remained unclear. Thankfully, combining it with ritonavir achieves sufficient drug level when dosed twice a day, plus this regimen should reduce the staggering 28 pills a day pill burden. Tipranavir faces many hurdles before approval, namely reformulation and finding the right drug combination to achieve maximal suppression of the virus. Encouraging laboratory data show that it shuts down viral replication for close to 90% of currently known drug resistant HIV strains. Because this drug tends to accelerate the major drug metabolic pathway, defining the drug interaction should be near the top of FDA's checklist when considering approval of the drug. —Charles A. Nelson

Potential side effects and toxicity: Trials have produced elevated levels of unconjugated bilirubin (without evidence of hepatoxicity) and cases of jaundice (yellowing of the skin or eyes) in some individuals taking atazanavir.
Tips: In head-to-head trials against Sustiva, both dosed once-a-day, and each combined with Combivir (twice a day), atazanavir has held its own at 48 weeks. The study consisted of 805 participents. The most promising news about atazanavir is that lipid abnormalities, often associated with the entire class of protease inhibitors, appear to be absent with this drug. Atazanavir did not result in a significant increase in blood levels of low-density lipoprotein (LDL or bad cholesterol). To date over 1,500 individuals have received atazanavir in clinical trials. (ICAAC 2002, abstract H-1076). Atazanavir should gain approval from the FDA in early 2003.

Photo not available because of experimental drug status.

Photo not available because of experimental drug status.

Class: experimental protease inhibitor
Standard dose: Dose not yet established because of experimental drug status, but Phase III studies are going forward with a dose of 400 mg once a day.
Manufacturer contact: Bristol-Myers Squibb, www.bmsvirology.com
AIDS Clinical Trials Information Service: 1 (800) TRIALS–A (874–2572)

Brand Name: Not yet established

Common Name: atazanavir

Doctor

No statement provided.

Activist

BMS experimental PI, atazanavir, is a single once-daily PI currently in phase III clinical development, the final stage of testing prior to marketing approval. The company is expected to seek FDA approval in the U.S. by April 2003. This PI requires careful monitoring and sometimes dose adjustments may be needed to help ease the adverse side effects associated with the PI class. As part of a HAART regimen with AZT and 3TC, through week 24, atazanavir or Sustiva increase fasting glucose, insulin or C-peptide levels when compared to the available PIs. Atazanavir is available through an early access program in the U.S. and in some other countries. —Charles A. Nelson

Brand Name: Fuzeon

Common Name: T-20, pentafuside

Photo not available because of experimental drug status.

Class: experimental fusion inhibitor
Standard dose: Dose not yet confirmed because of experimental drug status, but dose expected to be two 90 mg (1 ml subcutaneously) self-administered injections twice a day. No food restrictions (take with or without food). Take missed dose as soon as possible, but do not double dose.
Manufacturer Contact: Roche Pharmaceuticals and Trimeris, www.rocheusa.com and www.trimeris.com
AIDS Clinical Trials Information Service: 1 (800) TRIALS–A (874–2572)

Potential side effects and toxicity: Irritation or infection at site of injection, fever, and headache. Currently in Phase III clinical trials.
Potential drug interactions: Not yet reported.
Tips: T-20 is the first in a new class of anti-HIV compounds called fusion inhibitors. Fusion inhibitors block fusion of HIV with host cells before the virus enters the cell and begins its replication process. Because of injections, this drug will most definitely be used in the heavily-treatment experienced and salvage therapy options. Two large Phase III studies showed good viral load decrease when added to an optimized antiviral combination in heavily treatment-experienced people, including those with protease inhibitor-resistant virus and those who've taken all three current drug classes. Participants used 3 to 5 antivirals and both genotype and phenotype tests. Not everyone can add T-20 in addition to adding another medicine to which they are sensitive (no drug resistance). In both studies (with 500 participants in each), people on T-20 plus an optimized regimen had almost double the viral load log decrease as people on an optimized regimen alone (roughly 1.5 log decrease vs. .7 log decrease). T-20 is not expected to have cross-resistance with other HIV medicines. However, people simply adding T-20 to their current regimen may see resistance develop to T-20, and perhaps quickly. T-20's peptide structure may be recognized by the body as a foreign object, and then antibodies may be created to fight it. But this potential problem (not seen with other HIV drugs) has not occured. Because peptides are big molecules, they cannot be taken orally and must be injected. The size is another reason why T-20 might be recognized as a foreign object. May be able to penetrate lymph system, where most of the body's HIV hides. The FDA has given T-20 priority review, which means this drug could be approved by March 2003, if not sooner. However, according to Roche, this drug is very difficult and expensive to produce. Which could mean a number of things, including that the market price of T-20 will be higher than any anti-HIV drug ever brought to market and the potential problem of producing enough of the drug to make it available to everyone who might need it. Two twice a day creates pain and/or irritation at the site of injection in over 90% of study participants, but there has been less than a 3% drop out for this reason. To minimize injection site reactions (ISR), inject slowly and apply a gentle massage. Careful reconstitution of drug is also helpful. The drug must be carefully reconstituted for 30-45 minutes (for the two daily doses-refrigerate the dose that will be taken later). ISR may include itchiness, swelling, redness, pain or tenderness, hardened skin, and bumps. Injection sites include abdomen, upper arms and upper thighs. Follow instructions to avoid infection. ISR may worsen when injection is repeated in the same spot or given deeper than intended (for example, in the muscle). T-20 can be taken at the same time as other anti-HIV drugs.
Trimeris also has another fusion inhibitor in development, T-1249 in Phase II, that may work when/if resistance to T-20 develops. T-1249 will also be given as an injection but only once-daily, and there is talk of pegylating T-1249 (like interferon for hepatitis C is pegylated) to make it a once-weekly injection in the future.

Doctor

T-20 is an HIV fusion inhibitor that is expected to receive FDA approval by early 2003. By targeting fusion of the virus to CD4+ cells, T-20 is fundamentally different from previous antiretroviral agents that target an enzyme of HIV (either reverse transcriptase or protease). Because of this different target, current multi-drug resistance will likely be sensitive to T-20. However, as with all other antiretrovirals, drug resistance to T-20 can develop in the presence of persistent viral replication. A hurdle that the company has had to overcome is the actual manufacturing of the drug. T-20 is a large protein, and never before have large proteins been manufactured in the volume that T-20 will be. While many of these technical barriers have been overcome, there still may be shortages of T-20 after FDA approval. T-20 is also unique in that it will be the first approved antiretroviral that is an injectable drug, requiring a total of four injections twice-daily. —Jonathan Uy, MD

Activist

T-20's (now known as Fuzeon) development has sparked great interest in a new approach to interruption of viral replication. Fusion inhibitor is an important new class in HIV drug war. Used in combination with other antiretroviral drugs, T-20 is a potent inhibitor of multi-drug resistant HIV strains and provides a viable treatment option for individuals who find themselves close to the end of their rope. In TORO studies, the addition of T-20 in combination with Kaletra achieved a 0.8 log viral load reduction. Individuals naïve to Kaletra achieved a larger reduction in viral load than those with prior Kaletra experience. Perhaps the multi-drug resistant good news is premature. Scaling up product to meet the growing interest is still a major hurdle. Many activists have voiced concern that there will not be enough T-20 on-hand to meet the expected demand. Adherence to the dosing schedule will be critical to maximizing its success. —Charles A. Nelson

Drug Prices

by Enid Vázquez

For the last two HIV drug guides, the writer of Medicine Chest, Glen Pietrandoni (who specializes in HIV medicine at Walgreens through a small pharmacy inside a combination medical clinic and community service organization), provided readers with the Average Wholesale Price (AWP). This is the average price from which buyers (including pharmacies and drug programs) negotiate with pharmaceutical companies.

From there buyer sets the price for which they'll sell the drug. One retailer negotiates one price, Medicare negotiates another price, each state AIDS Drug Assistance Program (ADAP) negotiates a different price, etc. In the end, what your insurer ends up paying for your drugs is all over the map.

For the prices in this HIV Drug Guide, pharmacist Patrick Clay (of the University of Missouri-Kansas City School of Pharmacy and the Kansas City Free Clinic) conducted a survey of seven different pharmacies. Why? Because costs are all over the map. He then gives us an average.

Pietrandoni didn't like the idea of a survey, because some of the institutions surveyed cannot sell medicines to outpatients. Moreover, institutions usally have a lower price than you can get elsewhere.

But I think the word "wholesale" in the AWP might confuse readers. It's also usually much lower than what your insurer is going to pay for your meds, so the AWP makes the drug look a little more reasonable than it is.

Pietrandoni also notes that because most people get their medicine through insurance, price really does not make a difference to them. The vast majority of people are simply making a co-pay for each med (another price all over the map). Price is very important to those people paying cash and those with major medical plans covering their medicines rather than a prescription benefit.

But more importantly, he says, the price is the same no matter which pharmacy the person uses, because it's the person's insurance company or government program that has already decided what it will pay. The pharmacy does not set the price. However, beware of one thing. Says Pietrandoni, "In the case of cash or major medical insurance claims, it is the pharmacist who determines the price. This is where patients have to be alert."

Dr. Clay says he has "excellent" insurance—and a daughter who receives chronic asthma medicines with nebulizers. "It does make a difference in my 20% co-pay which pharmacy I go to. I pay less if I use mail order, online and then major chains. That is just a reality of medicine. The larger the buying group, the more likely a person is to get a better deal."

I think it's interesting to look at all the numbers Dr. Clay collected. For instance, the CostCo he surveyed charges $1,226.83 for Invirase, while DrugStore.com charges $562.87. But that CostCo charges $352.32 for Fortovase, while DrugStore.com charges $610.79. Strange, but interesting, isn't it? Must be all in the negotiation. (Pietrandoni points out—and Dr. Clay agrees wholeheartedly—that if you're making the same co-pay, try to use a pharmacy that specializes in HIV so that you can recieve better knowledge and service, not just bottles of medicine. Besides, there are lots of mistakes and less-than-ideal decisions being made out there, even by HIV specialist doctors, so it's good to have as many knowledgeable professionals on board as possible.)

So let's see how the monthly prices found in the Clay survey compares to the AWP. For the entire list, visit http://www.tpan.com. The pharmacies surveyed were the University of Illinois at Chicago; the University of Kentucky; DrugStore.com; www.Walgreens.com; www.Eckerd.com; a CVS, and www.CostCo.com.

Drug	Survey	AWP
Retrovir	$331.48	369.27
Videx EC	291.12	313.06 ($195.66 for 250 mg)
Hivid	238.57	284.43
Zerit	320.40	347.40
Epivir	297.73	316.04 (both 150 and 300 mg)
Ziagen	384.14	424.69
Combivir	630.37	685.28
Trizivir	1,038.33	1,109.96
Viread	410.46	432.00
Rescriptor	286.02	316.35
Viramune	327.80	360.59
Sustiva (600 mg)	412.04	449.64
Invirase	1,108.88	673.91
Crixivan	506.94	546.38
Norvir	690.80	771.54
Viracept	701.80	756.66
Fortovase	399.10	751.02
Agenerase	662.62	735.54
Kaletra	666.97	703.50

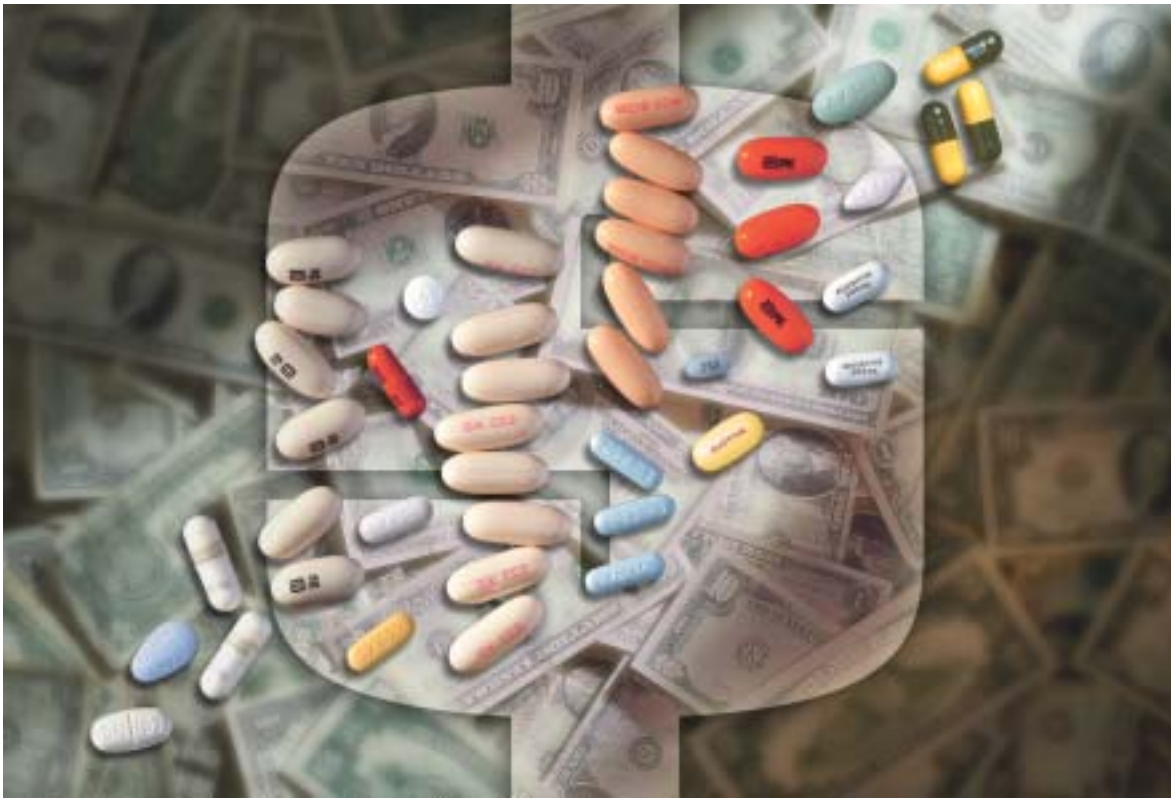
Insurance caps

What about those annual and lifetime caps that insurers put on medicines and medical care—should people with a cap be concerned about a $50 or $100 difference in the cost of a drug? This is what our two pharmacists had to say.

"$50 or $100 is about 5 to 10 percent difference in price," Pietrandoni points out. "In the big picture, unless you're paying for the full price of your medications, this is not that big of a worry. The problem comes in when some pharmacies charge the insurance (major medical) 180% of AWP or 200% AWP. This can happen when a pharmacy has the ability to charge whatever they like to the insurance companies. Large pharmacy companies do not do this because they cannot charge 'cash' customers one price and insurance customers another. Smaller pharmacies and mail order companies do not generally accept 'cash' customers and are at liberty to charge whatever they like.

"This does not hold true for persons with 'prescription cards,' where they pay a small 10 or 20 dollar co-pay. Those charges to the insurance company are dictated by the insurance company in advance. The price is the same no matter what pharmacy fills the prescription. This is what most people have." Pietrandoni also noted another interesting twist. "Patients should be aware of pharmacies offering special deals, like those advertising that patients don't have to pay their co-pays or deductibles. This is a good sign that the insurance companies will be overcharged to make up that difference."

Clay agrees to a certain degree. "The difference in clinical outcomes are not that great between regimens and individual [drugs], so it doesn't matter which one you start with." On the other hand, when you're paying out of pocket, "If you have limited resources, 50 bucks is 20 gallons of milk a month—that is huge." As for caps, "That was fairly common in early HMO plans, but as I understand it, it was challenged in court and lost. The impetus for the suit dealt with chemotherapy, followed by bone marrow transplant, etc."



Behind the Frontline
–A doctor looks at combos & side effects

Interview by Enid Vázquez

Dr. Tom Barrett is an HIV-specialist at Howard Brown Health Clinic here in Chicago. Howard Brown opened in 1974 as a health center for lesbians and gay men, an accepting place where their concerns could be voiced. When the HIV epidemic hit, Howard Brown became, of necessity, a place of expertise for treating people with the virus. Today the center also conducts extensive behavioral research, such as the use and effect of post-exposure prophylaxis (PEP) for sexual exposures, as well as vaccine and drug research. For this HIV Drug Guide issue, Barrett, a young gay doctor who grew up with the epidemic, talks about the meds in combination and some of their most common side effects. Note: what he discusses here and observes in his patients or clinic may not apply to you. As always, speak with your provider.

What drug combinations do you use the most?

I use a lot of once-a-day combinations. My patients generally find it easier to be compliant with a once a day regimen. There is a concern that if you miss a dose that the blood levels of the drugs will drop. But with once-a-day, you have half a day to remember a dose, as opposed to only six hours with twice-a-day. If you give patients the option, most will take once a day. If we want to manage this disease and maintain quality of life, we have to look at once a day therapy.

Once-a-day is harder to use in experienced people because of the resistance their virus has to some of the HIV medicines. A lot of these patients are on 4, 5, or even 6 drugs. But I have some experienced patients on once a day just because nothing else has worked, so we try to make it easier. The hope is that we can maintain their T-cells. Statistically speaking, their T-cells will start to drop over time. The question is how much time.

Sustiva/Combivir is still the most popular combination at our clinic. I have had people on Sustiva since it came out. Many people take it because twice-a-day is easier to remember—they take their medicine when they get up and when they go to sleep.

The question is always, if you use a drug first and you develop resistance, what does that mean for you down the road? We have a pretty good idea but a lot of our information is based on "test tube" data. We have quite a bit of data on the use of other protease inhibitors after a failure on Viracept. Viracept will fail to work with one specific mutation which does not affect other protease inhibitors currently on the market. However, it has another mutation which will give you cross-resistance to the other PIs.

I hope we will see once-a-day Trizivir in the future. That will make a big difference in how we treat a select group of patients. Imagine one pill once a day as compared to the numerous pills per day we used in the past.

What do you tell people about side effects?

What we really need to talk about is what's most likely to happen—in the first week, in the first month. I like to tell patients what I know they are going to get and warn them about the symptoms of the bad stuff in case it happens. We always have a talk about realistic expectations. I think it is important that they know what they are buying when they pick a certain regimen.

For example, Retrovir (AZT) has numerous potential side effects. The side effect that most of my patients get is nausea and fatigue that goes away in two to four weeks. I have had a few patients who have had anemia and neuropathy from AZT, however, they have been by far the minority.

If you get a side effect, the question is: can you live with it or not? The majority of side effects go away in a month or two. I have patients with a lot of peripheral neuropathy who say, 'Oh, it's nothing.' Then I have some patients who can't tolerate even small side effects. It is all about a patient's perspective and how it affects their lives. If we have options and a side effect is severe for a patient then we will switch out a drug. The whole idea is that you should be able to live your life with minimal interference.

The three biggest side effects I see in my patients are diarrhea when I use Kaletra or Viracept and nausea with AZT. I have had a fair number of patients who get a rash from Sustiva or Viramune.

We also see a number of patients with high cholesterol and lipodystrophy, and I don't think we always know the cause. I refer to our nutritional counselor regularly. Through dietary and supplement intervention we have minimized diarrhea and gastrointestinal side effects and I have had to use only a small number of cholesterol-lowering medications. While most of my patients don't feel the impact of high cholesterol in their daily life like they would nausea or a rash, it can have a huge effect later in life. We really try to look at the whole picture and keep our patients as healthy and as active as possible. The bottom line is that I need to manage my patient's expectations about certain drugs and try to match the right HIV regimen with the right patient. All of our regimens will work. The question is, will they work for you?

Common HAART Regimens	Common Side Effects	Less Common Side Effects
Combivir + Kaletra	nausea diarrhea increased cholesterol	vomiting neuropathy anemia
Combivir + Viracept	nausea diarrhea	vomiting neuropathy anemia
Combivir + Sustiva	nausea diarrhea vivid dreams poor sleep	vomiting neuropathy depression anemia
Epivir + Videx + Sustiva	vivid dreams poor sleep heartburn neuropathy	depression pancreatitis
Epivir + Viread + Sustiva	vivid dreams poor sleep	depression
Epivir + Viread + Viramune	rash	elevated liver function tests hepatitis
Epivir + Videx + Viramune	neuropathy heartburn rash	elevated liver function tests hepatitis pancreatitis
Videx + Viread + Sustiva	vivid dreams poor sleep neuropathy heartburn	pancreatitis depression
Videx + Viread + Viramune	rash neuropathy heartburn	pancreatitis elevated liver function tests hepatitis

Compiled by Dr. Tom Barrett for first-line regimens.

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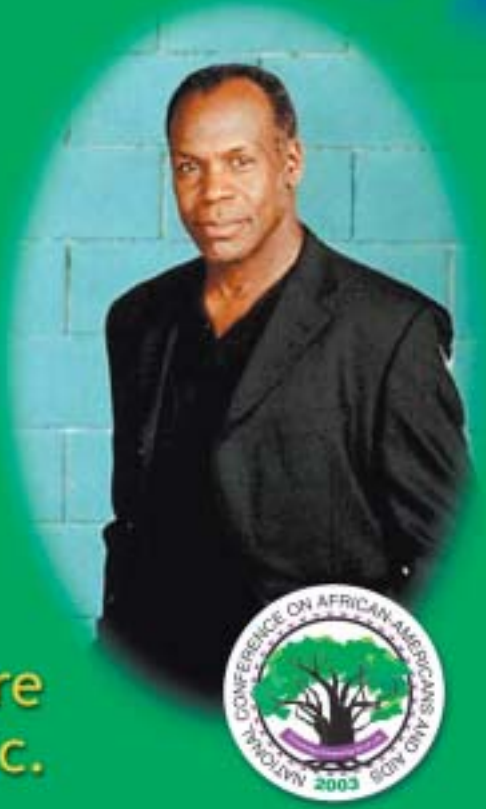

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Positively Aware 2002 Index

compiled by Jeff Berry

** indicates brief news item*

Topic / Article Title	Issue	Page
Activism		
Act the Fuck Up!	May/Jun	44
HIV Activism, it's Necessary	Mar/Apr	7
Larry Kramer gets liver transplant*	Mar/Apr	15
Children		
Children's Medications	Sep/Oct	42
Children's seizures*	May/Jun	19
Newborns and lactic acidemia*	May/Jun	20
Nkosi Johnson honored with children's Nobel prize*	Jul/Aug	21
Positive women's children have heart abnormality*	Nov/Dec	16
Scottish researchers find hiv-positive children have no-one to talk to*	Jul/Aug	20
Clinical trials		
AIDS and HIV related research/trials	Mar/Apr	30
FTC Superiority over d4T in Phase III Trial	Sep/Oct	48
SMART trial now enrolling*	Mar/Apr	16
Combination therapy		
Drug combos	Jan/Feb	62
Mixing and Matching Meds: ICAAC Update	Mar/Apr	21
Switching back and forth between different combos*	Jan/Feb	23
Triple nukes*	Nov/Dec	20
Viramune and Kaletra to spare the nukes*	Sep/Oct	19
Commentary		
A New Year—Reflections and continued hope	Jan/Feb	15
Drug Ads vs. Personal Responsibility	Jul/Aug	10
Fatty Acid	Jul/Aug	44
I Ride Because I Can—A Pos Ped Perspective	May/Jun	28
It Ain't Rocket Science	Nov/Dec	44
Keeping the Faith	Jan/Feb	9
Li'l Fucker	Mar/Apr	33
Love Stinks	Jan/Feb	66
Maggiore, Pregnancy and HIV	Jan/Feb	60
Of Birth and Dying	Nov/Dec	41
On the Watch	Jul/Aug	9
Perceptions: It's All in the Name	Jul/Aug	9
Positive Empowerment	Jul/Aug	22
Positive Empowerment	May/Jun	23
Positive Empowerment	Mar/Apr	29
Positive Empowerment	Sep/Oct	21
Positive Empowerment	Jan/Feb	58
Positive Empowerment: Talkin' 'bout My Generation	Nov/Dec	21
Positively Sesame Street	Sep/Oct	49
Random Musings	May/Jun	12
Seven's Up	Sep/Oct	52
Sex, Drugs and HIV	Mar/Apr	34
Test Positive Aware Network Turns 15	Sep/Oct	23
Trailblazers	May/Jun	11
When Does the Healing Begin?	Sep/Oct	22
Why Are There New Cases of HIV?	Mar/Apr	8
Commentary continued		
World AIDS 2002: On Condoms and Needle Exchange	Nov/Dec	12
Complementary therapy		
Living with Yoga	Jan/Feb	54
Conferences		
Conference news	Jan/Feb	23
ICAAC	Mar/Apr	17
ICAAC news*	Nov/Dec	19
ICAAC update	Jan/Feb	21
Retrovirus conference update	May/Jun	30
Update on the 9th Conference on Retroviruses and Opportunistic Infections	Jul/Aug	23
Deaths		
Creator of red ribbon dies*	Jul/Aug	21
Disclosure		
To tell or not to tell*	Jan/Feb	23
Dosing		
Triple, once-a-day combos for undetectable VL*	Jan/Feb	23
Drug compliance		
Adherence survey conducted*	Mar/Apr	15
Drug compliance		
Ten Ways to Mess Up Your Meds	May/Jun	40
Drug interactions		
Drug-nutrient Interactions and HIV	Jul/Aug	38
Sustiva label change*	Nov/Dec	16
Videx-EC/Viread combo*	Jul/Aug	20
Warning: Agenerase, methadone and the Pill*	Sep/Oct	17
Drug side effects		
Development of breasts in men*	Jul/Aug	21
Drug warning—severe muscular weakness*	Jul/Aug	19
Heart disease or HAART disease?*	Jul/Aug	23
Sustiva Electric Dreams	Mar/Apr	23
Treatment Options for Medication-induced Diarrhea	Jul/Aug	30
Viramune and the liver*	Sep/Oct	19
Women and non-nukes*	Nov/Dec	16
Drugs		
2002 HIV Drug Chart	Jan/Feb	36
Agenerase (amprenavir) fact sheet	Jan/Feb	48
Agenerase (amprenavir) study results*	Jul/Aug	25
Agenerase pro-drug*	Nov/Dec	20
Atazanavir moves into the spotlight while 083 bites the dust	Jul/Aug	42
Atazanavir study results*	Jul/Aug	25
Atazanavir vs. Sustiva*	Nov/Dec	19

Topic Article Title	Issue	Page
Drugs continued		
Atazanavir, new PI*	Jan/Feb	24
Combivir fact sheet	Jan/Feb	38
Combivir labeling mix-up*	Jul/Aug	20
Crixivan (indinavir) fact sheet	Jan/Feb	44
Crixivan vs. Fortovase*	Sep/Oct	29
DPC-083 experimental drug*	May/Jun	20
Drug tips	Jan/Feb	53
Drugs in development	Jan/Feb	52
Drugs on the horizon*	Mar/Apr	18
Entry inhibitors*	Jul/Aug	24
Epivir (3TC) fact sheet	Jan/Feb	34
FDA approves once-daily Epivir*	Sep/Oct	17
Fortovase (saquinavir) fact sheet	Jan/Feb	47
Fortovase/Norvir*	Sep/Oct	29
FTC expected to be approved in 2003*	Nov/Dec	15
Hivid (ddC) fact sheet	Jan/Feb	32
Integrase inhibitors*	Jul/Aug	24
Kaletra (lopinavir/ritonavir) fact sheet	Jan/Feb	49
Kaletra after four years*	Nov/Dec	20
Kaletra plus boosted Agenerase*	Nov/Dec	19
Kaletra study results*	Jul/Aug	25
Kaletra/Sustiva*	Nov/Dec	20
Nandrolone available*	Nov/Dec	19
Needle-free Serostim*	Mar/Apr	16
New Sustiva pill*	Mar/Apr	15
Norvir (ritonavir) fact sheet	Jan/Feb	45
Once-a-day Retrovir*	Sep/Oct	19
Once-a-day Viramune, Videx and Viread*	Sep/Oct	19
Open-label for T-20	Jan/Feb	64
PI mutations*	Mar/Apr	17
Rescriptor (delavirdine) fact sheet	Jan/Feb	41
Retrovir (AZT) fact sheet	Jan/Feb	30
Saquinavir once daily?*	Jul/Aug	25
Simplified treatments on the horizon?*	Jul/Aug	24
Sparing the PI's*	Jan/Feb	24
Sustiva (efavirenz) fact sheet	Jan/Feb	43
Sustiva beats a dual PI combo*	Sep/Oct	19
Sustiva beats dual PI's*	Sep/Oct	27
Sustiva vs. Viramune*	Nov/Dec	19
Sustiva vs. Viramune*	Jan/Feb	24
Switching from PI's to Ziagen*	Jan/Feb	24
Switching PI's*	Sep/Oct	28
Switching studies*	Mar/Apr	17
T-20 (Fuzeon) to come to market in early 2003*	Nov/Dec	15
T-20 (pentafuside) fact sheet	Jan/Feb	51
T-20 study results	Jul/Aug	25
Tipranavir fact sheet	Jan/Feb	50
TMC-125 experimental drug*	May/Jun	20
Trizivir fact sheet	Jan/Feb	39
Trizivir vs. Crixivan*	Jan/Feb	23
Videx/Videx EC (ddI) fact sheet	Jan/Feb	31
Viracept (nelfinavir) fact sheet	Jan/Feb	46

Topic Article Title	Issue	Page
Drugs continued		
Viramune (nevirapine) fact sheet	Jan/Feb	42
Viramune vs. Viracept*	Sep/Oct	27
Viread (tenofovir) fact sheet	Jan/Feb	40
Viread (tenofovir) study results*	Jul/Aug	25
Viread and resistance—at 2 years*	Jan/Feb	24
Viread data*	Mar/Apr	17
Viread resistance*	Sep/Oct	29
Viread stacks up*	Sep/Oct	18
Viread vs. Zerit*	Sep/Oct	18
What's New with Drug Regimens?	Sep/Oct	27
Zerit (d4T) fact sheet	Jan/Feb	33
Zerit XR study results*	Jul/Aug	25
Ziagen (abacavir) fact sheet	Jan/Feb	35
Financial issues		
Annual ADAP report*	Jul/Aug	21
Cost of medicines criticized*	Sep/Oct	18
Social Security Beneficiaries Returning to Work	Mar/Apr	24
The Ticket to Work Program: An Update	Nov/Dec	26
Hepatitis		
HCV/HIV Co-infection II: Sobriety and treatment	Mar/Apr	27
HCV/HIV Co-infection therapy	Mar/Apr	32
Hep C easier to transmit than HIV*	Jul/Aug	21
Hep C: Risk of Transmission and Treatment	Nov/Dec	29
Some HIV drugs may help treat hep B*	May/Jun	20
HIV complications		
Liver transplants*	May/Jun	19
HIV prevention		
CDC recommends gay men get tested*	Jul/Aug	20
Microbicides and HIV prevention	Nov/Dec	36
Microbicides: Prevention tool of the future	Jan/Feb	56
Risky behavior in San Francisco leads to increased rates of transmission*	Jul/Aug	21
HIV research		
Fauci wins prestigious award*	Jul/Aug	20
Genetic defects in baby monkeys exposed to HIV meds*	Jul/Aug	20
HIV transmission		
Barebacking survey*	Sep/Oct	17
Education campaigns lead public to lay blame on individuals for converting*	Jul/Aug	21
Perceived Safety Intensifies Danger for Gay and Bisexual Men	Sep/Oct	40
Undetectable cum?*	May/Jun	18
HIV treatment		
AIDS 2002: Still Room for Improvement	Jan/Feb	28
An HIV Treatment the World May Never See	Mar/Apr	19
Antiretroviral therapy 2002	Jan/Feb	27

Topic / Article Title	Issue	Page
HIV treatment continued		
Current controversies*	Sep/Oct	31
Expert Opinion from Barcelona	Sep/Oct	30
For experienced individuals*	Sep/Oct	30
Immune Reconstitution	Mar/Apr	36
New Treatment Guidelines	Sep/Oct	20
Once Again, One a Day	Nov/Dec	42
Once-a-day HIV Treatment: Ready for Prime Time?	Sep/Oct	44
Treatment Access as a Human Right	Sep/Oct	32
HIV vaccine		
An AIDS Vaccine: When?	Sep/Oct	43
Immune system		
Flu shots recommended*	Nov/Dec	19
Immune restoration	May/Jun	30
The Disconnect Sydrome	May/Jun	42
International issues		
Fighting AIDS with Peanuts	Sep/Oct	50
How the Global Fund Spent its Money	Sep/Oct	39
Hypocrisy*	Jan/Feb	22
Pan African movement*	Nov/Dec	16
South Africa ordered to provide HIV med*	Mar/Apr	15
South African doctors urge leaders to treat pregancy now*	Jul/Aug	45
The Politics of Africa's Pain	Sep/Oct	36
WHO: HIV drugs essential*	Sep/Oct	18
Interview		
One-on-one: Christopher Brown	May/Jun	33
Legal issues		
AIDS lawyers conference*	May/Jun	19
Former SF Health Commissioner must pay $5 mil for lying about status	Sep/Oct	17
Lipodystrophy		
Easy to read, not so easy to treat*	Jul/Aug	23
Exercise may help minimize*	May/Jun	18
Metabolic Toxicities and HIV	Nov/Dec	23
New-Fill for an Old Face	May/Jun	34
New-Fill achieves good results for researchers*	Jan/Feb	24
New-Fill on hold	Jan/Feb	64
Nutrition and lipodystrophy	Jul/Aug	33
Mental health		
Stress and HIV*	Jan/Feb	22
Minority issues		
African American HIV drama wins award*	Mar/Apr	15
NutritionHIV		
Drugs and Food	Jul/Aug	40

Topic / Article Title	Issue	Page
NutritionHIV continued		
Eating for Exercise	Jul/Aug	37
Treating Unintentional Weight Loss	Jul/Aug	28
Update on Micronutrient Needs in HIV	Jul/Aug	27
Opportunistic infections		
HPV in men*	May/Jun	19
Pets		
A Lad and His Dog	May/Jun	27
FIV vaccine for cats*	Nov/Dec	16
Policy		
President's Advisory Panel Finally Convenes	May/Jun	24
Pregnancy		
Birth defects from Sustiva*	May/Jun	18
Ethics guidelines changed for HIV-positive women using fertility treatment*	May/Jun	19
Viramune for pregnancy*	May/Jun	18
Prison issues		
Prison tales*	Mar/Apr	16
Re-infection		
Update*	Sep/Oct	18
Resistance		
Resistance rampant?*	Mar/Apr	17
Resistance to Anti-HIV Medications	Nov/Dec	33
What have we learned?*	Sep/Oct	30
Resources		
Positively Aware 2001 Index	Jan/Feb	70
Structured Treatment Interruptions (STIs)		
Conference news on STIs	Mar/Apr	36
On-and-off trial*	Jan/Feb	22
Substance use		
Acupuncture for treatment of cocaine addiction*	Sep/Oct	17
HIV and cocaine*	May/Jun	19
Vaccines		
News from International AIDS Conference*	Sep/Oct	31
Women		
20 Years of Women Living with HIV: Past, Present and Future	May/Jun	36
Lesbian HIV risk*	Nov/Dec	19
Pap/HPV guidelines*	Jul/Aug	21
Positive women and kidney problems*	May/Jun	19
Post-surgical risks found to be higher*	Jul/Aug	20

The Ever-Changing HIV Treatment Landscape

by Daniel S. Berger, MD

The landscape of therapy for HIV infection is always shifting, and the process by which treatment evolved has been fascinating. Just as artists derive their inspiration from many external, environmental, historical and cultural elements, physicians derive ideas and understanding of treatment options from many sources. Treatment history of the individual patient, what our patients themselves teach us, data learned from research derived through large multi-center trials and cohort studies, in addition to life's working experiences, all configure into formulating our knowledge base. Thus while our *oeuvre* of therapy is shaped by multiple influences, they likely include new studies being performed on agents in the pipeline, not yet available to most. Our experience derived by conducting cutting-edge clinical trials has been immeasurable. Although these studies are driven by pharmaceutical sponsors in order to arrive at the "holy grail"—bringing a drug to market, nevertheless, we have a high degree of respect and reverence for this form of industry hosted research.

Joseph Yoakum, the famous outsider artist of mixed Cherokee and African American parentage, became famous for his unique and original landscape drawings of the 20th century while working outside the mainstream. However, he eventually inspired many conventional and academically trained artists. Likewise, early on and during the first years of the HIV epidemic, HIV treatment also developed outside the mainstream of traditional pathways because of a desperate need for quick solutions. Out of this call for help, community research was born, not yet seen in other fields of medicine. Expanded access programs were implemented for treatments showing early promise in drug trials; this early availability became accepted and the norm for new HIV treatment—also not customarily witnessed in other medical disciplines. Finally, some of us as physicians formulated new treatment approaches, studied these ideas within the confines of our own clinics, and subsequently presented our research at juried national and international conferences, also adding to the influence upon which other doctors drew from. Therapy for HIV originally evolved as an art, developing as a dynamic during the latter part of the twentieth century. There is continued change in this dynamic as it occurs at present that will soon result in the next and forthcoming HIV treatment landscape.

Moreover, as the fields of immunology and virology matured, technology leading to drug development has grown in sophistication. Newer targets to attack HIV are being expanded. Entry and fusion inhibitors appear to be moving step-by-step in development and the future looks to their potential and widespread use. Integrase inhibitors, after many years of scientific work are finally advancing. Older drugs are also being reformulated into smoother work tools. Videx EC, Zerit XR and fos-amprenavir (the new formulation of Agenerase) are all newer, cleaned-up versions of previously marketed drugs. Additionally, new drugs in already existing classes are targeting specifically resistant virus, such that the rising problem of treatment failures is being tackled.

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Within the class of NRTIs there are currently six drugs. Three previously developed by GlaxoSmithKline (AZT, 3TC, abacavir) are reformulated in various one pill combinations of two and three agents together. Bristol-Myers Squibb (BMS) has reformulated ddI to Videx EC and soon a newer version of Zerit should be available within the next few months.

Triangle Pharmaceuticals has developed a new nucleoside, FTC, administered as one pill at once-daily dosing. While Triangle has already submitted this agent to the U.S. Food and Drug Administration (FDA) for approval, it should hit the market in eight to nine months. FTC is similar to 3TC, but its potency is somewhat greater. It does not however offer any advantages for patients with resistance to 3TC. A newer candidate compound, DAPD (amdoxovir) is another Triangle agent and appears effective against NRTI resistant mutations. On December 4, 2002, Triangle announced a take over bid by Gilead Sciences. With the Triangle pipeline in safe Gilead hands, DAPD's development should occur more quickly and efficiently.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

In the class of non-nukes (NNRTIs), two more agents are in the process of being developed, both touting benefit to patients

who have resistance to other agents of this class. Capravirine was once placed on the back burner due to potential toxicity. While animal studies demonstrated new onset vasculitis problems in dogs, Pfizer's Agouron division has satisfied FDA concerns and was able to re-invigorate their research into developing capravirine. TMC 125, Tibotec-Virco's potent NNRTI, has shown potent antiviral activity in the face of multiple NNRTI-associated mutations, including the K103N. Johnson & Johnson has recently acquired Tibotec-Virco; we hope this move can provide support for drug development of Tibotec-Virco candidate agents.

Nucleotide Reverse Transcriptase Inhibitors

Tenofovir (Viread) became the first anti-HIV nucleotide to be available for widespread use one year ago. The design of tenofovir's pivotal trials was unique to the industry in that the drug studies testing its safety and effect was demonstrated through intensification type protocols. Study patients had tenofovir added to their existing stable regimens; the results demonstrated a persistent durable benefit. Tenofovir has become very popular by physicians prescribing it for their patients because of its strong potency, low side effect profile, administration as one pill once-daily dosage and effectiveness against resistance. However, Gilead Sciences is working on a new and similar nucleotide agent, GS 7340, which, if effective, has the potential for penetration into lymph nodes at very high concentrations. The implications for such a treatment, if successful, are quite large. Understanding the molecular and structural basis of this agent may enable more compounds to be developed with potency and activity in various viral sanctuary sites, such as the lymph nodes and the potential for enhancement of immune reconstitution.

Protease Inhibitors (PIs)

Several newer protease inhibitors are in the HIV drug pipeline, each posing specific advantages over previously developed agents. Atazanavir, now available through expanded access by BMS, appears to lay claim for being able to avoid the hyperlipidemia problems that other PIs are plagued with. Thus patients being treated with atazanavir may go without elevations in blood lipids, such as cholesterol and triglycerides.

Tipranavir (Boehringer-Ingelheim Pharmaceuticals) a novel non-peptidic agent, appears to retain its potency against many PI-resistant mutations, but will require boosting by ritonavir, as many other older PIs do. TMC 114 (Tibotec-Virco) also has activity against many resistant mutations of protease inhibitors. With the help of these two new very promising agents, patients exhausting their options with existing protease inhibitors can continue deriving effective treatment from this highly potent drug class.

Entry and Fusion

Newer targeting sites against the virus are finally emerging. Both fusion and entry inhibitors have emerged as one of the most promising classes of drugs in development for patients who have been exposed to multiple agents. Their mechanism of action differs from other existing classes in that their activity occurs outside the cell; they inhibit binding of the viral envelope to specific binding sites on CD4+ T-cells.

continued on page 76

The ever-changing HIV treatment landscape has led to many more treatment combinations while using newer sites of attack

Present Treatment Landscape	Future Treatment Landscape
NRTIs	
AZT	AZT
ddC	ddC
ddI	ddI-EC
d4T	d4T XR
3TC	3TC
abacavir	abacavir
	FTC
	DAPD
NNRTIs	
nevirapine	nevirapine
efavirenz	efavirenz
delavirdine	delavirdine
	capravirine
	TMC-125
Nucleotide	
tenofovir	tenofovir
	GS 7340
PIs	
saquinavir	saquinavir
ritonavir	ritonavir
indinavir	indinavir
nelfinavir	nelfinavir
amprenavir	Fos-amprenavir (908)
lopinavir/ritonavir	lopinavir/ritonavir
	atazanavir
	tipranavir
	TMC 114
Fustion/Entry Inhibitors	
	T-20
	SCH-C
	T-1249
	PRO-542
Integrase Inhibitors	
	L-870810
	S-1360

Radical Red

Liberation Theology

by Laura Jones

"No one wants to have a sore spot touched, and therefore a society with so many sores twitches when someone has the courage to touch it and say: 'You have to heal that. You have to get rid of that…' " Archbishop Oscar Romero, 1978.

This column's title is something of a misnomer, in that I'm really not all that "radical" (I'm also not naturally red, but any roommate of mine could have told you that). Oscar Romero wasn't really all that radical either—at least not when he was first installed as Archbishop of El Salvador in February of 1976. But within little more than a year, Romero began to say and do very "radical" things for an Archbishop, even though what he said and did was only consistent with the words and actions of Jesus himself. After a fellow priest was shot by a member of the El Salvadorian military for helping peasants organize for their own self-determination, Oscar Romero began to preach what's called "Liberation Theology" and use his position within the Church to challenge the violence perpetuated upon the peasantry by the power elite. This theological approach to confronting the violence in late-1970s El Salvador led to nuggets like these:

"When we speak of injustice here below and denounce it, they think we are playing politics. It is in the name of God's just reign that we denounce the injustices of the earth." 1977

"A civilization of love that did not demand justice of people would not be a true civilization; it would not delineate genuine human relations. It is a caricature of love to try to cover over with alms what is lacking injustice, to patch over with an appearance of benevolence when social justice is missing. True love begins by demanding what is just in the relations of those who love." 1979

"I would like to make a special appeal to the men of the army, and specifically to the ranks of the National Guard, the police, and the military… No soldier is obligated to obey an order contrary to the law of God. No one has to obey an immoral law." 1980

Reading those words, people familiar with the teachings of Jesus might wonder what the big fuss was. After all, nothing Oscar Romero advocated was new; in fact, it's pretty much all present there in the four books of the Gospel. However, ten days after appealing to Catholic soldiers to stop killing peasants, members of the El Salvadorian military (financed and trained with U.S. tax dollars) shot Archbishop Romero dead while he prepared the offertory for Communion.

Apparently Liberation Theology was a little more than the power elite were willing to deal with just then.

Liberation Theology is a specific Christian approach to addressing the politics of systemic oppression and poverty. However, the basics also work nicely as an approach to confronting the root violence of the HIV/AIDS pandemic—and you don't have to be a Christian to use them, either.

We have in HIV/AIDS a global tragedy that takes complete advantage of the worst we impose upon others and ourselves. Heterosexism and homophobia. Racism. Sexism and misogyny. Institutionalized poverty, often linked to legacies of colonialism, slavery, and other forms of economic exploitation. And, without doubt, the internalized "-isms" that lead so many of us to self-medicate with drugs and alcohol, take risks with our own emotional or physical health, or act out against those over whom we hold some margin of power.

Effectively fighting HIV/AIDS means being willing to confront and overthrow these institutionalized social ills, even when we ourselves benefit from maintenance of the status quo. It means dismantling heterosexism and homophobia, even though it's comforting for heterosexuals to live in a world that tells them they're good and everyone else is going to hell. It means doing away with racism, even though that involves loss of the enormous privileges conferred upon white people by discrimination against people of color. It means fighting sexism, even though a social structure that guarantees men more power than women makes the world very pleasant for men. It means fighting the political and economic institutions that keep people imprisoned in lives of perpetual poverty, even if those systems benefit us personally through business profit.

Equally important is the task of confronting our own internalized oppressions. This is especially true for people living with HIV/AIDS, who are all too frequently encouraged to hate themselves in a million small (and huge) ways. Voices ranging from "What did you expect?" to "You are evil and deserve everything this disease can do to you" can follow very closely on the heels of the voices that tell us we also "deserve" the ill effects of the social institutions described in the previous paragraphs.

continued on page 76

Combination Dosing Adjustments

by Glen Pietrandoni R.Ph.

The International AIDS Society-USA and the U.S. Department of Health and Human Services are continuously updating guidelines to help physicians and patients choose the best ways to use drugs in combinations for treating HIV/AIDS. You have probably seen the "one from column A and two from column B" charts that have been around for years. These tables have been a wonderful tool to determine treatment options for those newly diagnosed and treatment naïve. This is the basis of most treatment decisions for a patient's first few drug regimens. How do physicians use the list of drugs to choose a drug regimen for patients with limited drug options? Sometimes drugs can be arranged together in ways to get more potent regimens, to cut down on pill count, or simply because there are no other choices at the time.

In the United States, it is the standard of care today to use phenotype and genotype testing to see which drugs are effective in halting viral replication in a particular patient. After a few drugs or drug classes are eliminated due to resistance (drug doesn't work any longer), it may be more difficult to find a drug regimen that fits neatly on the DHHS guideline chart. Because HIV medicine is as much an "art" as it is a science, your provider may need to combine drugs together that normally would not be used in the same cocktail. When certain drugs are combined, adverse reactions can occur, but drug interactions are not always bad things. Again, sometimes agents can be combined to our benefit. The best example of this is when Norvir (ritonavir) is combined with other protease inhibitors. The drug level of these protease inhibitors are higher and last longer when taken with Norvir than using the drug without Norvir. The benefits often include better viral control and lower pill burden. The downside of throwing all these drugs together can mean an increase in side effects if the blood levels go too high. Always communicate with your health care team to let them know what's going on. Remember, while most side effects can be managed and are temporary, more serious complications may require a change in therapy. There still needs to be that target of 95% adherence to achieve maximal viral suppression and get those T-cells up!

The combination drug chart shows some optional ways to combine drugs with each other. Some combinations have more data to support their use, while other combinations are only now being studied for the first time. Some of these regimens are not yet FDA approved, but many physicians treating HIV/AIDS have experience in using regimens "off label" with some success. As always, learn about your treatment options and discuss the benefits and disadvantages of a new regimen before you start taking the medication.

Glen Pietrandoni is director of Clinical Pharmacy Services for the Walgreens Specialty Pharmacy, focusing on HIV, located in the Howard Brown Health Center of Chicago. Contact: Glen.Pietrandoni@walgreens.com.

KEY

RTV Norvir (ritonavir)	DLV Rescriptor (delavirdine)
LPVrKaletra (lopinavir/ritonavir)	DDI Videx (didanosine, ddI)
NFV Viracept (nelfinavir)	EFV Sustiva (efavirenz)
IDV Crixivan (indinavir)	QD once daily
SQV Fortovase, Invirase (saquinavir)	BID twice daily
APV Agenerase (amprenavir)	TID three times daily
NVP Viramune (nevirapine)	Q8H every 8 hours

Combination Drug Chart

Compiled by Glen Pietrandoni, R.Ph.
Key on page 72

Norvir (ritonavir) RTV with:	Tips:
Agenerase (amprenavir)	
600 mg APV BID + 100 mg RTV BID	
1200 mg APV QD + 200 mg RTV QD	
Crixivan (indinavir)	
400 mg IDV BID + 400 mg RTV BID	Take with food
800 mg IDV BID + 100 mg RTV BID	Take with food
800 mg IDV BID + 200 mg RTV BID	Take with food
Fortovase (saquinavir sgc)	
400 mg SQV BID + 400 mg RTV BID	
800 mg SQV BID + 200 mg RTV BID	
1000 mg SQV BID + 100 mg RTV BID	Can use Invirase
1600 mg SQV QD+ 100 mg RTV QD	Can use Invirase
800 mg SQV BID + 100 mg RTV BID + 600 mg EFV QD	
Viracept (nelfinavir)	
750 mg NFV BID + 400 mg RTV BID	
Sustiva (efavirenz)	
600 mg EFV QD + 500 mg RTV BID	
600 mg EFV QD + 800 mg SQV BID + 100 mg RTV BID	
600 mg EFV QD + 1200 mg APV BID + 200 mg RTV BID	
Viramune (nevirapine)	
200 mg NVP BID + 600 mg RTV BID	
Rescriptor (delavirdine)	
600 mg DLV BID + 600 mg RTV BID	May reduce RTV to 400 mg or 500 mg BID if side effects

Kaletra (lopinavir, ritonavir) LPVr with:	Tips:
Agenerase (amprenavir)	
750 mg APV BID + 533 mg/133 mg LPVr BID	New data suggests using this combination with caution because of decreased lopinivir levels
Crixivan (indinavir)	
600 mg IDV BID + 400 mg/100 mg LPVr BID	Take with food
Fortovase (saquinavir, sgc)	
800 mg SQV BID + 400 mg/100mg LPVr BID	
Viracept (nelfinavir)	
750 mg NFV BID + 400 mg/100 mg LPVr BID	
Sustiva (efavirenz)	
600 mg EFV QD + 533 mg/133 mg LPVr BID	
Viramune (nevirapine)	
200 mg NVP BID + 533 mg/133 mg LPVr BID	

Viracept (nelfinavir) NFV with:	
Agenerase (amprenavir)	
1200 mg APV BID + 1250 mg NFV BID	
Crixivan (indinavir)	
1200 mg IDV BID + 1250 mg NFV BID	
Fortovase (saquinavir sgc)	
1200 mg SQV BID + 1250 mg NFV BID	
800 mg SQV TID + 750 mg NFV TID	
Sustiva (efavirenz)	
600 mg EFV QD + 1250 mg NFV BID	
Viramune (nevirapine)	
200 mg NVP BID + 1250 mg NFV BID	
Crixivan (indinavir) IDV with:	**Tips:**
Agenerase (amprenavir)	
750 mg APV TID + 800 mg IDV TID	
Kaletra (lopinavir/ritonavir)	
400 mg/100 mg LPVr BID + 600 mg IDV BID	Take with food
Norvir (ritonavir)	
400 mg RTV BID + 400 mg IDV BID	Take with food
100 mg RTV BID + 800 mg IDV BID	Take with food
200 mg RTV BID + 800 mg IDV BID	Take with food
Sustiva (efavirenz)	
600 mg EFV QD + 1000 mg IDV Q8H	Empty stomach
Viramune (nevirapine)	
200 mg NVP BID + 1000 mg IDV Q8H	Empty stomach
Rescriptor (delavirdine)	
400 mg DLV TID + 600 mg IDV Q8H	Empty stomach
Fortovase (saquinavir soft gel capsule) SQV with:	
Agenerase (amprenavir)	
750 mg APV TID + 800 mg SQV TID	
Rescriptor (delavirdine)	
600 mg DLV BID + 1600 mg SQV BID	
400 mg DLV TID + 1200 mg SQV TID	
Agenerase (amprenavir) APV with:	
Sustiva (efavirenz)	
600 mg EFV QD + 1200 mg APV TID	
600 mg EFV QD + 1200 mg APV BID + 200 mg RTV BID	
Norvir (ritonavir)	
600 mg APV BID + 100 mg RTV BID	
1200 mg APV QD + 200 mg RTV QD	
Viread (tenofovir) with:	
Videx-EC (didanosine, ddI)	
300 mg Viread QD + 250 mg ddI QD	

Can You Feel What I Feel?

by Jim Pickett

"Statistics are human beings with the tears wiped away."

The above gem is courtesy of Dr. Terry Tafoya, the executive director of Tamanawit, an international, multicultural consulting company that specializes in sexuality, grief, loss, Native American heritage and spiritual healing. A Native American from the Taos Pueblo and Warm Springs Nations, Tafoya is a clinical psychologist and traditional storyteller, and lucky for those of us in attendance, was one of the featured plenary speakers at the Illinois state conference on HIV and STDs this past fall.

"Statistics are human beings with the tears wiped away."

Tafoya did not claim this beautiful insight as his own, indicating he had heard it from a nurse with whom he was working. But he passed it along to us, and I have repeated it over and over to myself, and anyone who'll listen, since.

Statistics, percentages, numbers, forecasts, demographics, epidemiology, targeted populations, populations at risk, disproportionately impacted populations data, data and more data. While all of it is important, while all of it is absolutely vital to the work we are doing, absolutely crucial to the understanding of the depth and complexity of this fucking epidemic from hell we as a planet are experiencing, the data and the percentages and the statistics and the numbers numb us. Numbers such as "over 42 million" infected worldwide. The numbers like 45% prevalence in Botswana. The numbers like 45,000 new infections every year in the United States. The numbers. The numbers. Numb. Us. What does "over 42 million" mean?

We know the anguish and the sting of those tears. We have wet our faces. We have felt our hearts breaking. Our tears have come from desolation and from rage, from pain and fear, and from release and utter joy. We have tasted them. And they were bitter or they were sweet. Or they were both. And we will taste them, again.

We are infected ourselves. We have loved ones who are infected. We are lovers, husbands and wives, brothers, sisters, mothers and fathers and friends. We are caregivers and care receivers. We are doctors, nurses, case managers, outreach workers and volunteers. We are educators and public speakers, we are advocates and activists and lobbyists. We are funders and fundraisers. We are executive directors and board members. We wear red ribbons. We raise awareness. We walk, we run, we ride. We stitch. We bitch. We fight back, we fight complacency, we fight ignorance and discrimination and racism and homophobia. We fight poverty. We fight AIDS. We yell, we holler, we scream and shout. We write letters, we send e-mails, we make calls, we get out to get the vote and we vote.

We make love, not war.

We make war.

We fuck like it's the end of the world.

We annoy them by surviving.

We are outraged because we are paying attention.

We bleed.

And we cry. But who sees our tears? Do we wipe them away before anyone takes notice? Do we turn our head? Do we excuse ourselves? Are we ashamed? Do we hide? Do we wipe our tears away before anyone takes notice, before anyone can begin to really understand our pain our anguish our release and our joy? Before anyone can have the opportunity to feel what we feel, to empathize, to try our shoes on for size, to begin to really, truly understand? Do we wipe our tears away, blow our nose, and leave just the bare data, the cold hard facts, the percentages, the stats, along with a snotty Kleenex? Do we dry our eyes and leave compassion, empathy and understanding, humanity, our humanity, to go thirsty? Do we allow only part of the story to be revealed?

45,000 new infections in a year is a statistic.

One is a tragedy.

More now than ever, with the intense political and ideological pressures we are facing, including the Republican-controlled Congress and the extreme conservatism that is threatening the work we all do, those of us directly impacted by this plague, infected and affected, you and I, have a duty. We must make it real. Our suffering and the suffering of those we serve must not be silent. It must not be hidden behind a veil of normalcy, or beneath a burqa of banality if you will. We must not hide behind effective drug regi-

The Buzz continued

continued from page 70

T-20 (Fuzeon) is the first fusion inhibitor to be developed and is currently available through a limited expanded access program; it should be approved for widespread use early in 2003. T-20 has been shown to decrease viral load significantly (approximately 0.7 log), sustained in patients who are the most challenging to treat because of a high degree of resistance to multiple existing antiviral drugs. This effect, unparalleled in these advanced disease patients, was observed in addition to the effect of optimization of patients' background antiviral treatment. While T-20 is injected twice daily subcutaneously, most patients reported this to be an easy task; only 10% found this to be difficult. Efforts are underway to develop a longer acting form of the drug so that less frequent injections may be necessary. Trimeris and Hoffman-LaRoche are also developing T-1249, which acts on a larger area of the cell surface.

Schering-Plough is involved with developing entry inhibitors that are orally bioavailable (thus will be taken orally). These drugs interfere with virus attachment to the target cells before the fusion step takes place. SCH-C's activity is dose related and is continuing in Phase I. Studies to elicit any drug interactions or pharmacokinetic effects with other known antiviral compounds are proceeding before Phase II will be initiated. Progenics Pharmaceuticals' entry inhibitor appears to be synergistic with other fusion inhibitors and also looks promising.

Integrase Inhibitors

Integrase is a new target within the viral replicative cycle that has previously been difficult to attack. Many candidate compounds were identified early on but virtually all were failures for differing reasons. Now however, three compounds have the potential to enter into further clinical testing. Two competing pharmaceutical companies involved in their development are Merck and GlaxoSmithKline.

Preliminary testing of one such compound, L-870810 (Merck) has shown safety and very potent effect. A study design of Rhesus macaques (a type of monkey) infected with an aggressive simian immune deficiency virus (SIV) was observed to demonstrate very powerful suppression of this virus. Because the mechanism of action for this class of drug targets a new and different enzyme, there should not be any issues of previous cross-resistance. Additionally, this agent is metabolized by glucuronidation. Thus, not being affected by p450 enzyme pathway used by PIs, it should pose little or any drug interactions.

Conclusion

We are in limbo, but moving at a good pace: antiviral treatment for chronically infected individuals are in the process of being refined drastically. Community research and cohort studies were once criticized because there was an insufficient degree of bench and basic scientific research and lacked concerted attention. The movement and progress in HIV treatment was once thought to be occurring in various independent directions and on many fronts not organized. Placed in the context explained in this article, these directions paradoxically achieved strength and a focal point towards finding solutions to many of the common problems of treating complicated patients. This transformation in the expressionistic landscape of treatment continues to be positive in its evolution.

Daniel S. Berger, MD is Medical Director for NorthStar Healthcare, Clinical Assistant Professor of Medicine at the University of Illinois at Chicago and editor of AIDSInfosource (www.aidsinfosource.com). He also serves as medical consultant and columnist for Positively Aware. *Dr. Berger can be reached at DSBergerMD@aol.com or (773) 296–2400.*

Pickett continued

mens, behind smiling faces, behind gym-pumped bodies, behind bathroom doors. We are not seeing people turn into skeletons before our very eyes, as we once did. There is no compelling visual that lets the general public know what a horror AIDS truly is, at least not readily apparent in this country. We must illustrate our outrage, for not everyone is paying attention as we are. And everyone should be. Local concerns are global. Global concerns are local.

We must not allow political agendas to silence our realities and cause even more harm.

We must represent what we are going through, we must be intimate, we must provide the context, we must give details. We must also talk—a lot—about what works and what doesn't work. I am thinking about prevention and comprehensive sexuality education here. There is not a shred of science behind the shit storm of abstinence-only propaganda. Who are we telling? It's not up to someone else, it's up to us.

One new infection is a tragedy.

We must share our stories and make visible our tears.

How do they taste? Are they bitter, sweet, or both?

It's up to us.

Visit www.vote-smart.org

Call the Capitol switchboard at 1–800–648–3516.

Radical Red continued

continued from page 71

But the truth is this: none of us are under obligation to participate in our own destruction, especially by our own hand. Those of us who carry heavy loads of self-hatred, who hurt ourselves emotionally or physically, need to hear that decree and hand-deliver it to the little militia unit inside us that serves to keep us down. We need to understand that oppressing ourselves is no more acceptable than oppressing others.

The people who benefit most from institutionalized disparity are the ones with a vested interest in everyone's participation in these systems of oppression, whether internalized or externalized. They get to go drink fizzy lemonade while we silence, drug, beat, or kill ourselves and the people we're conditioned to de-humanize. And since that distribution of power is unacceptable, I challenge all of us to do something "radical" indeed: believe in our own self-worth and the self-worth of every individual, and then act upon that belief.

TPAN Calendar of Events

All events held at TPAN unless otherwise indicated.
For additional information on these events please contact Michael Barnett at (773) 989–9400.

January 2003

Date	Time	Event
Wednesday, 8th	7–9 PM	"Committed to Living Series - Drug Resistance" Speaker: Dr. Jonathan Uy of University of Illinois - Chicago
Tuesday, 14th	7–9 PM	Chicago Bar Olympics Opening Ceremony - at Charlie's in Chicago
Wednesday, 15th	7 PM	Client Advisory Board Meeting
Monday, 20th		TPAN Closed, Martin Luther King, Jr. Day
Tuesday, 21st	7:30 PM	TPAN Monthly Board Meeting at Ann Sathers in Chicago
Thursday, 30th	6–10 PM	"January Chill" Party Positive at Berlin in Chicago

February 2003

Date	Time	Event
Wednesday, 5th	7–9 PM	"Committed to Living Series - Nutrition" Speaker to be announced
Fri-Sun, 7th–9th		Fireball Weekend, www.fireball.com
Tuesday, 11th	7–9 PM	TPAN Tuesday at @mosphere in Chicago
Tuesday, 18th	7:30 PM	TPAN Monthly Board Meeting at Ann Sather's in Chicago
Thursday, 27th	6–10 PM	End of the Month Party Positive at Berlin in Chicago

Programs and Meetings

All meetings held at TPAN unless otherwise indicated:
5537 North Broadway, Chicago.
Office hours: Monday–Thursday, 9 am–8 pm. Friday, 9 am–6 pm
phone: (773) 989–9400 • fax: (773) 989–9494
e-mail: programs@tpan.com • www.tpan.com

Support groups sponsored by the
Chicago Department of Public Health
Peer Support and Buddy programs sponsored by the
AIDS Foundation of Chicago

Monday

TPAN Daytimers

A group for people with HIV who prefer to meet during the day. Mondays and Thursdays at 10:30 am.

Newly Aware

A group for newly diagnosed individuals. Mondays at 7:30 pm. 2nd and 4th Mondays include HIV 101 education.

Straight Talk

A group for HIV-positive heterosexuals. Mondays at 7:30 pm.

Tuesday

Living Positive

HIV-positive gay men discuss how being positive affects relationships and deal with the impact of HIV as single men. Tuesdays at 7:30 pm.

Positive Progress

A group for HIV-positive people in recovery. Tuesdays from 7:00–9:00 pm.

Wednesday

Medical Clinic

Free medical care provided by a nurse practitioner. This program is in conjunction with the Needle Exchange Program and is offered by Access Community Health Network. Call for an appointment. Wednesdays 10:00 am–6:30 pm.

Needle Exchange Program

Free, anonymous, legal syringe exchange and HIV/AIDS prevention. Every Wednesday 5:00 pm–7:00 pm at TPAN office. In association with Chicago Recovery Alliance.

Yoga

Wednesdays at 7:30 pm.

Thursday

TPAN Daytimers

A group for people with HIV who prefer to meet during the day. Mondays and Thursdays at 10:30 am.

Medical Clinic

Free medical care provided by a nurse practitioner. This program is in conjunction with the Needle Exchange Program and is offered by Access Community Health Network. Call for an appointment. Thursdays 2:00 pm–5:00 pm.

Brothers United in Support (BUS)

A group for HIV-positive gay and bisexual men of African descent. Thursdays at 7:00 pm.

Staying Strong, Healthy and Empowered (SSHE)

A group for HIV-positive women. Call Kathleen at (773) 989–9400 for more information.

Party Positive Social at Berlin

Berlin, 954 W. Belmont, Chicago. Thursdays from 6:00–10:00 pm.

Friday

Safe Passage

A group for young adults (ages 18–24) who are HIV-positive. Fridays at 7:00 pm.

Scheduled By Appointment

Family AIDS Support Network (FASN)

A group for family, friends, and caregivers. Call Betty Stern at (773) 989–9490.

Speakers Bureau

Individuals are available to community groups and organizations to educate on HIV, safer sex, harm reduction and experiences of living with HIV. Call Rodney at (773) 989–9400.

Peer Support Network

Provides one-on-one support for recently diagnosed individuals. Volunteers provide support, information and referrals. Call Rodney at (773) 989–9400 to get a buddy!

Positive Buddy

Volunteers provide individuals living with HIV/AIDS one-on-one emotional / physical support. Call Rodney at (773) 989–9400 to get a buddy!

Miscellaneous

ChicagoPos18to24 at aol.com

AOL chat room for young adults (ages 18–24) who are HIV-positive. Hosted by TPAN's Young Adult Program. Go to AOL town square. Monday through Friday 3:00 pm–5:00 pm.

Special Thanks to Sidetrack and Stoli for sponsoring the TPAN 2002 Holiday Party

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