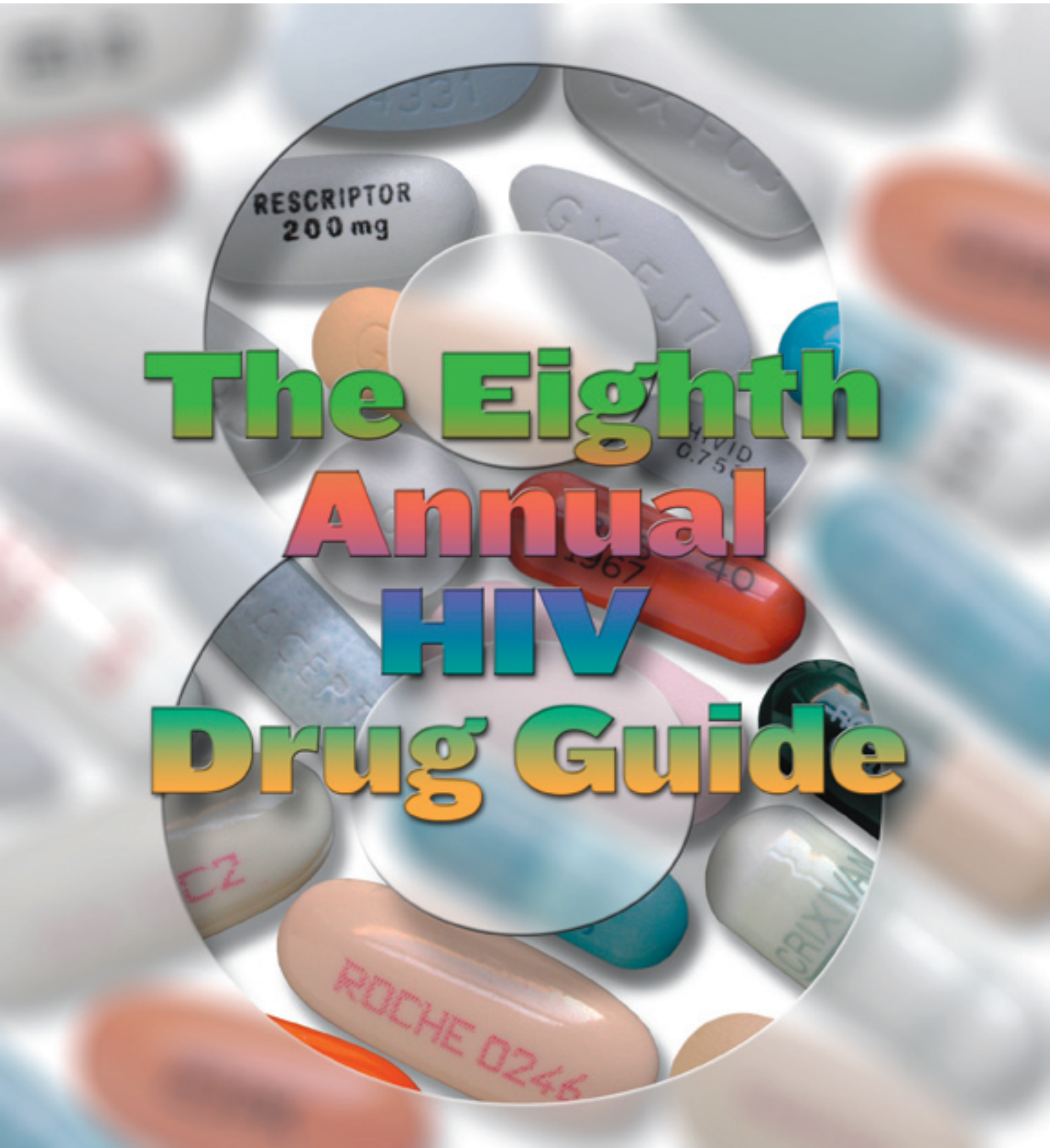
January / February 2004

Positively Aware

The Journal of Test Positive Aware Network



The Eighth Annual HIV Drug Guide

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Time Flies

Another year has come and gone, all too quickly. It seems like only yesterday that we were frantically putting the finishing touches on the 2003 HIV Drug Guide. While we have made so many advances in our understanding and treatment of HIV, so much remains unknown.

World AIDS was front and center in the media throughout 2003. Following the 2003 Drug Guide, we also turned our attention to China, South Africa and Ecuador (Mar/Apr) and ended the year focusing on Eastern Europe, Vietnam and Botswana (Nov/Dec). AIDS is a worldwide pandemic. Access to and costs associated with antiretroviral therapy, care and treatment remains a huge problem in many parts of the globe.

However, HIV is still "alive and well" here in the United States as well. While our government polices the globe, too many individuals right here at home are dealing with reduced or no healthcare coverage, escalating insurance premiums with reduced access to care, and unaffordable drugs. HIV continues to rage at uncontrollable rates in the African American community. The rates of new HIV-infections are on the upswing among gay men across the country. People in the rural and southeast regions of the U.S. are testing positive at alarming rates. There are far too few services and support networks available for them. Club drugs, recreational drugs and injection drug use are creating dangerous liaisons in many communities (Jul/Aug).

In the fall of 2003, we published a special issue of *Positively Aware*, "Positive Parenting" (September/October), which turned out to be one of the most popular issues in years. Once thought to be impossible, more and more HIV-positive men and women are creating life and raising healthy and happy children.

As we move into 2004 there are many questions that remain unanswered:

- What's the status on research into new drug classes that will be useful for treatment experienced and naïve people?
- Will the new drugs be any better against cross-resistant viruses?
- How do we improve our knowledge on managing drug side effects, toxicities and drug-drug interactions?
- When should people start taking antiretroviral therapy, and who should interrupt therapy and when?
- How does one manage lipodystrophy and other metabolic complications of living long term with HIV?
- How does one treat HIV/HCV and other co-infections?

As always, we remain committed to bringing you, our readers, the most accurate and up-to-date HIV treatment information as soon as possible.

We open the year 2004 with our 8th Annual HIV Drug Guide. This issue brings you the latest information on the twenty-two currently FDA approved anti-HIV drugs. This year, as in past years, the drugs are listed by class in the order that they were approved by the FDA. This year's Drug Guide benefited from the knowledge of the following individuals. Dr. Stephen L. Becker, with the Pacific Horizon Medical Group in San Francisco, who wrote "New Targets, New Drugs, Failed Trials" and provided the doctor's comments for this year's publication. Deneen Robinson, a treatment educator and former columnist for *Positively Aware*, contributed "What's New in HIV" and the activist's comments for the Drug Guide. Dr. Daniel Berger provides an insightful analysis of new strategies to attack the virus. Matt Sharp gives us a good overview of the revised Department of Health and Human Services (DHHS) Guidelines.

An excellent panel of pharmacists was convened by returning contributing editor Patrick G. Clay, Pharm.D. *Positively Aware* thanks the following experts for their volunteer contribution to the guide: Tom Chin, BScPhm, Pharm. D., Clinical Pharmacy Specialist, St. Michael's Hospital, Toronto; Monica Shieh, Pharm. D., Detroit Receiving Hospital; Mark Bernstein, Pharm. D., Gilead Sciences; Michael L. Lim, Pharm. D., HIV Clinical Development & Medical Affairs, GSK; Jennifer Justice Kiser, Pharm. D., Antiretroviral Clinical Pharmacology Fellow, University of Colorado School of Pharmacy; Guy Boccia, Pfizer Inc.; Cynthia Feucht, Pharm. D., BCPS, Clinical Infectious Diseases Pharmacist; Louis Stokes Cleveland Veterans Affairs Medical Center; Christopher McCoy, Pharm.D., Clinical Pharmacy Coordinator, Infectious Diseases Specialist, Beth Israel Deaconess Medical Center, Boston; Lynne Spearbraker, Pharm. D., Clinical Pharmacist, Aurora Sinai Medical Center, Milwaukee; Eric G. Sahloff, Pharm. D., Assistant Professor of Pharmacy Practice, University of Toledo, College of Pharmacy; Linda W. Kam, Pharm.D., Infectious Disease Clinical Specialist; James A. Haley, VA, Tampa; Kristi M. Kuper, Pharm.D.; Eli Korner, Pharm.D., MPH, Kaiser Permanente of Colorado; Deanna Merrill, Pharm. D., MBA, CDE, National Coordinator, Chair Consortium for HIV/AIDS Inter-Regional Research; Beulah P. Sabundayo, Pharm.D., MPH, The Johns Hopkins University School of Medicine; Nafeesa Chin-Beckford, Pharm.D., Jackson Memorial Hospital, Miami; Shellee A. Grim, Pharm.D., University of Illinois at Chicago; Jean Lee, Pharm.D., McAuley Heath Center, Grand Rap-

Photo © Russell McGonagle

ids; Monika N. Daftary, Pharm.D., Assistant Professor and Ambulatory Care Pharmacist, Howard University School of Pharmacy; Cindy Perfect, Pharm. D., The Medical Center of Central Georgia; Marisel Segarra-Newnham, Pharm. D., MPH, VA Medical Center, West Palm Beach; and Raymond Pecini, Pharm.D. and Medical Liaison, Roche Laboratories.

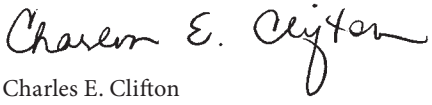
Chin-Beckford, Pharm.D. advises, "Each HIV drug is only one part of your drug regimen. You'll need to take all your medications to get the full benefit of the therapy and to reduce the risk of resistance. Do not let your medications run out. The amount of virus in your blood could increase drastically if you stop. Always consult your healthcare provider before stopping your meds. The common side effects that can occur will usually go away within a few weeks. So hang in there! Also, your doctor should be notified of all medications that you are taking, both prescription and non-prescription (over-the-counter, including herbal ones)."

Remember that pharmacists are also great sources of information. In addition, for more information on possible drug interactions, visit a great website at the University of Liverpool: www.hiv-druginteractions.org.

And last but not least, I would like to especially thank my supporting cast—Enid Vázquez, Jeff Berry, Matt Sharp and Dr. Daniel Berger for their dedication to this cause and hard work on this issue and every issue of *Positively Aware*. And a big thanks to Russell McGonagle for making us look good every issue and for putting up with our constant rewrites [*A privilege I have grown to love very much!—RM*].

In the course of this year, we lost several friends and some brilliant AIDS activists, who stood strong for many, many years, to AIDS and other complications. Please take a moment to reflect on the importance of your life and on those individuals who mean the most to you. Time flies.

Be Strong. Stay Safe.



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

The 2004 Chicago Area HIV Services Directory is now available.

2004 CHICAGO AREA HIV SERVICES DIRECTORY

This free directory contains over 370 agencies that provide services to individuals living with or impacted by HIV. Free copies are available for pick up or delivery.

Call Carlos A. Perez at (773) 989-9400, ext 233. or e-mail your request to: directories@tpan.com.

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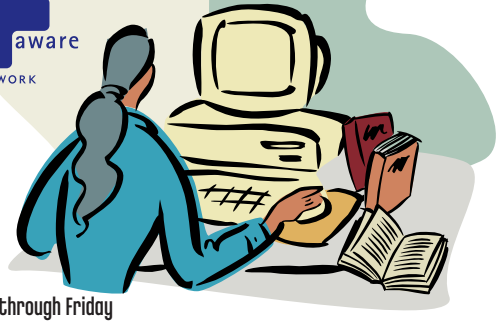

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Chicago Ride for AIDS June 5 & 6. Call 773.989.9400 for information

New Targets, New Drugs, Failed Trials and the Need for More Information

by Stephen L. Beckler, MD

This past year has seen the approval of the first drug directed against a novel HIV target. This of course is T-20, or enfuvitide. T-20 marks the first new class since the protease inhibitors were introduced in late 1995. While T-20 has provided some heavily treatment experienced patients with the means of constructing an effective and enduring antiretroviral regimen, its twice daily subcutaneous injection, cost and limited availability will markedly limit its widespread use. Nonetheless, it paves the way for a new generation of virus entry and fusion inhibitors. Many of these agents will be orally administered and will no doubt provide the means of interdicting the viral life cycle for many patients. One can only hope that their eventual cost will remain in the range of the majority of currently available antiretroviral agents, and thus be widely affordable for patients receiving their care in the public as well as private sector.

This year also saw the approval in the U.S. and Europe of two new protease inhibitors (PI) and one nucleoside reverse transcriptase inhibitor (NRTI).

Among these agents, the PI atazanavir (Reyataz) has garnered the most attention. Atazanavir appears to be effective in both treatment-naïve and, when boosted with ritonavir, in some treatment-experienced patients. Atazanavir is dosed once daily, well tolerated, and has remarkably little effect on serum cholesterol or triglycerides. Each of these features clearly distinguish it from the majority of approved PIs. Care must be taken when using atazanavir with other HIV agents, notably tenofovir. Also, it cannot be used at present with anti-acid agents (studies are underway), including proton pump inhibitors such as Prilosec or H2 blockers such as Pepcid AC, Zantac or Tagamet.

The other PI approved this year is the pro-drug of amprenavir (Agenerase). Called Lexiva (fos-amprenavir), this formulation greatly reduces the pill burden and gastrointestinal side effects of amprenavir. Lexiva has demonstrated impressive effectiveness in advanced (low CD4, high viral load) patient populations. Lexiva has been tested in treatment-naïve and experienced patients, and can be used either once or twice daily with or without ritonavir boosting. (All treatment-experienced patients should use it twice daily and with ritonavir.)

A new nucleoside analogue was approved this year as well. Emtriva (FTC or emtricitabine) is a NRTI much like lamivudine (3TC or Epivir). It has an identical resistance pattern, safety profile, and like 3TC can be dosed once daily. It will soon be combined with tenofovir (Viread) into a combination pill much like Combivir.

Failed trials

Several important clinical trials have improved our understanding of the most effective combinations of antiretroviral therapy. Combinations containing three NRTIs, so called triple nukes, have been found to be inferior to three drug combinations using at least two classes of antiretroviral agents.

In an important study that was terminated early, the triple nuke combination of AZT, 3TC and abacavir (all in one drug, Trizivir) was found to be significantly less effective than an efavirenz (Sustiva)-based regimen in treatment-naïve patients. While Trizivir clearly still has a place among the drugs used to treat HIV, it is also clearly not as effective when used as the whole regimen and not part of anti-HIV therapy.

Two other seemingly potent triple nuke regimens fared far worse than Trizivir in studies. Unlike Trizivir, the performance of these combinations was so dismal that they should never be used as sole treatment. The combination of tenofovir, abacavir and lamivudine was dramatically less effective than the combination of efavirenz with abacavir and lamivudine. Didanosine (ddI or Videx) when used with tenofovir and lamivudine was effective in only one of the 30 patients who received this combination. Clearly more work is needed to understand why these otherwise effective agents failed so miserably.

Drug of choice

The guidelines for treatment of HIV infection issued by the Department of Health and Human Services for the first time listed combinations of agents to be used in the treatment of naïve patients. This recommendation was based on the evaluation of these combinations in clinical trials. Among the preferred combinations are those of

- efavirenz (Sustiva) with Combivir, or
- efavirenz with stavudine (d4T or Zerit) and lamivudine (3TC or Epivir), or
- efavirenz with tenofovir and lamivudine.

Recommended among the PIs is

- Kaletra with Combivir, or alternatively
- Kaletra with stavudine and lamivudine.

This is not to say that other triple drug combinations are not effective, but rather that these combinations have not shown the same effectiveness, safety and durability as the preferred combinations.

Drugs on the horizon

Several important agents are in advanced (Phase III) clinical trials. These include the PIs tipranavir and TMC-114. Both agents are felt to be effective in those patients harboring significant PI-resistant virus. If these agents prove effective they should become available in expanded access in 2004 and 2005.

Clinical trials are of course the means by which new agents are tested for effectiveness and safety. It is also the venue for testing against the current standard of care agents. Participation in clinical trials is a very important part of the learning and discovery process, especially for HIV agents.

It is of vital importance that participants in clinical trials be of a diverse racial/ethnic and sexual mix. By participating in clinical trials we can not only speed along the process of drug development and approval, but learn valuable lessons about how the drugs work in different patient populations. If a clinical trial meets your particular needs, consider participation. You can avail yourself of important treatment options, but also assist all clinicians and researchers in the HIV field by providing crucial clinical information. In turn, you'll be helping people with HIV around the world.

Dr. Stephen L. Becker is with Pacific Horizon Medical Group in San Francisco, and on the faculty of the University of California, San Francisco.

Special thanks to Gilead Sciences for supporting Dr. Becker's work on the 8th Annual HIV Drug Guide.

what's new in HIV?

by Deneen Robinson

The science of HIV has continued to marvel us with an ever-changing landscape of new information that keeps us guessing as to what is next. The truth is that this virus will always challenge us. We will never be bored. There will always be something new to learn or teach others. We know that antiretroviral therapy is effective in treating HIV disease. However, as people on HIV treatment age, their options become more limited and the need to bring new drugs to market is increasingly important. In addition, women's access to appropriate care, with specialists who not only understand HIV, but healthcare for women is still an issue. We need to continue to get women and people of color into treatment and clinical trials, in roles other than victims.

New Treatments

The recently approved Lexiva, T-20, Emtriva and Reyataz have given us a few more choices for people who are treatment experienced. Unfortunately, because of the timing of approval and the problem of HIV resistance, there have not been enough drugs to give us a complete regimen of at least three new drugs for treatment-experienced people. As time goes on and people experience multiple resistance, it is more and more difficult to find compounds that will work. The pipeline offers promise for those people.

Tibotec-Virco, a Belgian pharmaceutical company recently purchased by Johnson and Johnson, has two remarkable drugs in development that are designed to meet this need. TMC-114 is a second-generation protease inhibitor designed to be active against protease resistant mutations. *In vitro* data shows that TMC-114 has potent activity against both wild type and resistant forms of HIV. The drug has demonstrated greater efficacy if boosted with ritonavir. Although the trials have been small (50 people), the results look promising and have allowed the manufacturer to move to the next stage of clinical development. TMC-125 is a non-nucleoside reverse transcriptase inhibitor (NNRTI) also produced by Tibotec-Virco that has demonstrated *in vitro* that it can work in the presence of the K103N mutation. K103N is the mutation that causes one to lose the entire class of NNRTIs. The future of treating HIV disease depends on the creation of novel compounds that are successful in the presence of multiple resistance.

Superinfection

At the 2003 International AIDS Society (IAS) conference in Paris, superinfection was discussed with clinical data to prove its existence. According to additional information presented at IAS, we now have people who have tested positive with no treatment options. This news has a number of implications. Those who test positive with no treatment options have to wait for new compounds in the same way people were waiting for options in the early years of AZT. It also means that the hope for a vaccine is even more elusive due to the difficulty of creating a vaccine that encompasses all the known mutations and the possible mutations that may occur in the future. Finally, as the number of people who have superinfection increases, mortality may increase as well.

Women and HIV

There has been a great concern about the number of women who are testing positive for HIV. Interestingly, since the early 1980s, women have been present among the numbers of people both living and dying from HIV disease. The sudden fascination with women has yet to translate to equal participation of women in clinical trials, expanded access programs and access to care. In early 2003, Dr. Kathleen Squires presented a paper on the relationship between HIV, gender and treatment. Women are still the last to be treated and the lowest number of participants in clinical trials. Interestingly, she pointed out that women are as capable as men in handling antiretroviral therapy.

For years women have been saying that there are differences in how women respond to antiretrovirals. In this document, Dr. Squires indicates that women do experience greater side effects or more severe side effects to some of the currently used antiretrovirals. In order to minimize these problems women should be consistently part of clinical trials. Also, the different side effects that women are experiencing should be investigated and physicians and other health care providers should be made aware of this information. These differences should be implemented into the care plans of women living with HIV. We should stop paying lip service to these issues. If we truly want to do something, we should consistently do the "extra" work required to ensure the participation of women in all aspects of HIV care.

It means ensuring that the voices of women are heard even if they are not able to disclose their status. It also means that we address the barriers to health care by providing day care, food vouchers, bus tokens, etc. Finally, it means listening to the

issues that women have raised and allowing the voice of women to be more than the accepted few that we have been listening to up to this point. It means ensuring that the voice of women continues to grow until there is equal representation.

For those of us who have always been the stakeholders, it means sharing your "territory" with someone who has as much right to be at the table as you. Most importantly, it means that stakeholders take the responsibility of bringing someone else along, so that there is always a voice at the table that reflects the unique needs of all populations impacted by HIV.

African Americans and HIV

In addition to the constant hype about women, we are touting that African Americans are the new "face" of HIV. It boggles the mind. African Americans have always been disproportionately impacted by HIV. Always. For those of us who have been around since the epidemic began, we know what the myth has been. "HIV is a gay, white male disease." Instead of dispelling that rumor, that myth has actually been the catalyst for much of the denial that occurs in the African-American community about their HIV risk. Unfortunately, it is very difficult to fix something this huge. Now what has happened since we have begun to talk about African Americans has been a decrease in funding, waiting lists for AIDS Drug Assistance Programs, flat funding of Ryan White and limited pharmaceutical dollars for community organizations. On observation that does not make sense. What are we doing to deal with the societal issues that have caused this new incidence? What are we going to do for the large number of people who are going to be accessing care? More importantly, how are we going to pay for it?

The one thing that women and African Americans have in common is limited resources to pay for costly medical care and AIDS drugs. In light of the large number of underpriveleged people accessing services and society's expressed concern for these groups, why are we limiting money for services instead of increasing it? It brings to mind the idea that now that the epidemic has become more associated with poverty and other societal ills, we are treating it just like we have consistently treated the poor in this country. We treat them with disrespect.

We show our disrespect for this "new" group of infected individuals by not ensuring that they are a part of the "cure." Going forward, why don't we try to ensure that these groups are included in trials and ensure that they have equal access to medical care and treatment?

The saying goes, "The more things change, the more they stay the same." As the arsenal of medications to treat HIV has grown, we are still perplexed about finding new ways to treat HIV disease. As the advancements in understanding this virus have grown, we still have yet to discover an effective way to create a vaccine. We have learned that HIV has a way of changing its outer core to elude antibodies. We have learned that HIV replicates at such a rapid rate that the body is always behind in trying to kill the newly created virions.

We have a number of novel ways of treating HIV in the pipeline. The success of creating T-20 has opened the door for other entry inhibitors. There are a number of different types of entry inhibitors that, if successful, will give us more ways of suppressing this virus. The reality of a cure is still far off. The more we learn about HIV, the more the difficulty of finding a cure seems. There are a number of companies manufacturing vaccine options. Our greatest hope for a vaccine is a number of years in the future. In the meantime, we are going to have to work on ways to keep people healthy until the cure or better treatment options are available.

The host

The host for HIV is very complicated. Each of us is unique with our own problems and clinical deficiencies. These differences make it difficult for us to develop a simple formula of treating HIV disease. Clinicians are learning that understanding the host is the key to successfully treating HIV disease. As we pay attention to host factors such as family disease histories, risk for cardiovascular disease, cultural differences and gender differences, we are better able to find the most appropriate treatment for the person living with HIV. We have a number of trials that are exploring host issues such as TDM—therapeutic drug monitoring. The TDM trials are trying to see the impact on viral suppression if we dose medications based on the unique issues of the host. We'll see what the results show. Also as we learn more about HIV disease, we are including host factors as ways to measure someone's risk for hyperlipidemia and high glucose in people living with HIV.

Perhaps the newest reality is that the more we learn, the more we realize we need to learn. The most important idea is that we need to be vigilant in this fight. The future of treating HIV disease is for all of us to continue to advocate for new treatments and better care for those living with HIV.

Deneen Robinson is an African American woman who has been working in the field of HIV education for seven years. She has been living with HIV for 11 years. She says that, "During this time, my ability to access and understand information has been the most powerful tool in my personal fight against HIV." She is a resident of Dallas, and a graduate of the African American AIDS Institute in Los Angeles. Shortly after finishing work on the Drug Guide project she accepted a position as Advocacy Relations Manager with Abbott Laboratories.

Brand Name: Retrovir

Common Name: zidovudine (ZDV), 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 (may be taken with or without food). Clear, strawberry-flavored liquid available for pediatric use. Take missed dose as soon as possible, but do not double up on your next 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: Most common side effects include 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 is pancreatitis (inflammation of the pancreas), hepatomegaly (enlarged liver) with steatosis and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in all patients taking NRTIs but is more common and more severe in women, people who are obese and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distention, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver (called hepatomegaly with steatosis).

Pancreatitis can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting and blood in the urine. Your physician will check for pancreatitis by checking for increased levels of amylase and lipase in the blood. Risks for pancreatitis include: higher than recommended doses of NRTIs, advanced HIV, and alcohol use. The risk for pancreatitis with AZT is low compared to didanosine.

Potential drug interactions: Biaxin (clarithromycin), Dilantin (phenytoin), 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, ganciclovir (Cytovene and Vitrasert), valganciclovir (Valcyte) and Depakote (valproic acid) increase AZT blood levels, and perhaps toxicity. 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, sulfadiazine, 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. Together they may also increase the risk of lactic acidosis.

Tips: Taking with food may minimize upset stomach. Do not use with Hydrea or Droxia (hydroxyurea). AZT has somewhat of a bad rep left over from its early years when the doses given were too high. Studies show that AZT crosses the blood-brain barrier to a useful degree, which may be beneficial for patients at risk for neurological damage (such as dementia) from HIV. 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).

Doctor

The oldest and historically most widely used antiretroviral, zidovudine (ZDV) has a place in many HAART regimens. While not as potent and arguably with a greater frequency of toxicity than the newer generation of NRTIs, ZDV remains an important agent. ZDV has been found effective in decreasing work-related and mother-to-child transmission of HIV. However given the recent documentation of the frequency of transmission of drug resistant virus, there may be better options for the acute or chronically infected, treatment naïve patient than a regimen containing ZDV. One area that requires further investigation is whether the inclusion of a thymidine analog, either ZDV or d4T, might favorably alter the pathway of viral resistance in regimens containing newer combinations of NRTIs. Should this be demonstrated, then ZDV will likely be a component of many of our future HAART regimens.

—Stephen L. Becker, MD

Activist

AZT was created initially as a cancer drug. In the 1980s, AZT was administered in very large doses to treat HIV and caused lots of side effects. As a result many in the community remain leery about using it. However, the manufacturer has reformulated the drug and it is as effective without the high level of toxicity. In its current dosage, however, it causes anemia in a large number of people. It can also cause discoloration of nail beds in African-Americans. Despite these issues, AZT has shown itself to be very useful as a backbone drug because it works well with other nucleosides, except Zerit (d4T). AZT should never be used with d4T. GlaxoSmithKline suggests that physicians closely monitor obese women and patients with risk factors for liver disease while they are on AZT.

—Deneen Robinson

1x

Brand Name: Videx & Videx EC

Common Name: didanosine, ddI

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One 400 mg enteric coated (Videx EC) delayed-release capsule once-a-day, with adjustments for weight (also available in 125 mg and 200 mg caps). For the older formulation of Videx, standard dose is two 100 mg buffered tablets twice-a-day (or four tablets once daily). Videx is also available as a buffered powder for oral solution. Take Videx and Videx EC strictly on an empty stomach, 30 minutes before or two hours after food or drink, except water. Take missed dose as soon as possible, but do not double up on the dose.
Manufacturer contact: Bristol-Myers Squibb, www.bmsvirology.com, 1 (800) 272–4878
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) may go away once didanosine is stopped, but can be painful and permanently debilitating if not treated in time. Upset stomach (nausea and vomiting), diarrhea, headache, and more rarely pancreatitis (inflammation of the pancreas) has also been reported. Other toxicities include eye changes and optic neuritis (inflammation of nerves in the eye). 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. Rare but potentially fatal toxicity with all NRTIs is pancreatitis (inflammation of the pancreas), hepatomegaly (enlarged liver) with steatosis and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in all patients taking NRTIs but is more common and more severe in women, people who are obese and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distention, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver (called hepatomegaly with steatosis).

People with a history of peripheral neuropathy, pancreatitis or heavy alcohol use should avoid didanosine. Pancreatitis can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting and blood in the urine. Risks for pancreatitis include: higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Body fat redistribution/accumulation has also been reported with didanosine.

Potential drug interactions: The levels of didanosine are increased by 50% when given at the same time as Viread (tenofovir), therefore a dose reduction to 250 mg for Videx is recommended. The dose of didanosine may need to be increased when taken with methadone. The combined use of didanosine and zalcitabine (Hivid) is not recommended because of the higher incidence of peripheral neuropathy. Antineoplastics (anti-tumor treatment) such as AZT and hydroxyurea may increase risk of peripheral neuropathy. Combining didanosine with stavudine (Zerit) or with hydroxyurea (Hydrea), alcohol, Cytovene, or NebuPent may increase risk of pancreatitis. Also, Cytovene substantually increases didanosine levels. Videx 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, but 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 or bite/chew). The capsules eliminate the bad taste and texture of the tablets and the enteric coating reduces diarrhea. Absorption can be decreased by as much as 50% when taken with food, so always try to take on an empty stomach. Antacids containing magnesium or aluminum may cause adverse side effects if given at the same time as Videx tablets. If you have reduced kidney function, you may require a lower dose. Notify your doctor immediately if peripheral neuropathy is suspected.

Doctor

ddI is another agent developed early in the HIV epidemic and, like AZT, in many respects has stood the test of time. Available in a once daily, enteric formulation ddI has modest potency and a predictable toxicity pattern. Peripheral neuropathy and pancreatitis are the two significant adverse events. ddI requires dosing adjustment when used with tenofovir (see above). This agent has a place in initial therapy as well as in treatment-experienced patients. It was previously felt that the 3TC-associated mutation, M184V, impaired response to ddI. This has been demonstrated not to be so, making ddI a viable agent for those failing prior therapy containing 3TC.

—Stephen L. Becker, MD

Activist

When asked about Videx my first thought is the large chalky tablets and their bad taste. They also eat away at the enamel on your teeth. Thankfully, Bristol-Myers Squibb created a form of Videx that is coated—Videx EC (enteric coating). Videx EC eliminates diarrhea as a side effect, although some may still experience other gastrointestinal upsets. Videx EC and Videx have to be taken on an empty stomach. Videx/Videx EC and Zerit (d4T) should not be taken together due to the higher risk of pancreatitis and neuropathy. Remember, never to take Videx with an antacid. Also, Videx should not be administered with AZT or Hivid due to higher incidence of peripheral neuropathy.

—Deneen Robinson

3x

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 (may be taken with or without food). Liquid available through compassionate use program. Take missed dose as soon as possible, but do not double up on your next 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) may go away once Hivid is stopped, but can be painful and permanently debilitating if not treated in time. Other side effects include headache, fever, skin eruptions, sores or swelling in the mouth, nausea, and pancreatitis. Rare but potentially fatal toxicity with all NRTIs is pancreatitis (inflammation of the pancreas), hepatomegaly (enlarged liver) with steatosis and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in all patients taking NRTIs but is more common and more severe in women, people who are obese and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distention, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver (called hepatomegaly with steatosis).

People with a history of peripheral neuropathy, pancreatitis or heavy alcohol use should avoid Hivid. Pancreatitis can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting and blood in the urine. Your physician will check for pancreatitis by checking for increased levels of amylase and lipase in the blood. Risks for pancreatitis include: higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Body fat redistribution/accumulation has also been reported with Hivid. With few exceptions, these side effects are stronger than is seen with other NRTIs.

Potential drug interactions: Due to increased risks associated with peripheral neuropathy, Hivid should not be taken with Videx (ddI) or Zerit (d4T). Epivir (3TC) should also be avoided as it can lower the levels of Hivid in the body. Other medications that can interact with Hivid include Antabuse (disulfiram), Fungizone (amphotericin B), Benemid (probenecid), Chloromycetin (chloramphenicol), certain chemotherapy agents, Dilantin (phenytoin), dapsone, Foscavir (foscarnet), isoniazid, Flagyl (metronidazole), hydralazine, ribavirin, and Macrodantin/Macrobid (nitrofurantoin). When used at the same time as 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 jiroveci* pneumonia (PCP), may increase risk of pancreatitis. Hivid should not be taken at the same time with antacids containing magnesium or aluminum, as they may decrease levels of Hivid in the body.

Tips: Hivid should be avoided if you are pregnant or breast feeding. 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 is, for good reason, a rarely used NRTI. Its toxicity pattern, primarily peripheral neuropathy greatly limits its use. Better agents are available for patients in all stages of HIV infection.

—Stephen L. Becker, MD

Activist

ddC is one of the earliest nucleoside reverse transcriptase inhibitors. Today it is hardly ever used except in salvage situations. Because of the lack of clinical data and overlapping toxicities, among the NRTIs ddC is only recommended to be used with AZT. Its major side effect is neuropathy, which occurs in one-third of patients on the drug. The neuropathy may resolve with reduced doses or discontinuation.

—Deneen Robinson

2x

Brand Name: Zerit

Common Name: stavudine, d4T

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 (may be taken with or without food). Zerit is also available in 15 mg, 20 mg, 30 mg and 40 mg capsules and a powder for oral solution; check for food restrictions. Take missed dose as soon as possible, but do not double up on your next dose.
Manufacturer contact: Bristol-Myers Squibb, www.bmsvirology.com, 1 (800) 272–4878
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) may go away once Zerit is stopped, but can be painful and permanently debilitating if not treated in time. 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. Other side effects include headache, chills/fever, malaise (general ill feeling), insomnia, anxiety, depression, rash, upset stomach (nausea and vomiting), diarrhea and abdominal pain. Rare but potentially fatal toxicity with all NRTIs is pancreatitis (inflammation of the pancreas), hepatomegaly (enlarged liver) with steatosis and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in all patients taking NRTIs but is more common and more severe in women, people who are obese and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distention, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver (called hepatomegaly with steatosis). People with a history of peripheral neuropathy, pancreatitis or heavy alcohol use should avoid Zerit. Pancreatitis can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting and blood in the urine. Stop taking Zerit immediately if exeriencing symptoms of pancreatitis and seek immediate medical attention. Your physician will check for pancreatitis by checking for increased levels of amylase and lipase in the blood. Risks for pancreatitis include: higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Stop taking Zerit immediately if experiencing symptoms of pancreatitis and seek immediate medical attention. Lipodystophy ("buffalo hump"), fat loss (lipoatrophy) in the face and limbs (arms and legs), and central fat accumulation has been associated with Zerit. Zerit is the HIV drug most implicated by studies as causing lipoatrophy. Also seems to be implicated in blood lipid (fat) increases, particularly triglycerides.

Potential drug interactions: When used in combination with Zerit, drugs such as Fungizone (amphotericin B), Foscavir (foscarnet), dapsone, and other drugs used to treat HIV may increase the risk of developing peripheral neuropathy. Cytovene and Vitrasert (ganciclovir), valganciclovir (Valcyte), intravenous Pentam (pentamidine), and Videx (ddI) may increase the risk of pancreatitis. Should 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. Because of additive neurotoxicity, if possible, Zerit should not be combined with zalcitabine (Hivid) or ddI.

Tips: Contact your healthcare provider immediately if peripheral neuropathy is suspected, but do not stop taking medication unless directed to do so by your healthcare provider. Studies show that Zerit crosses the blood-brain barrier to a useful degree, which may be beneficial for patients at risk for neurological damage (such as dementia) from HIV. Many leading HIV advocates are adamant that Zerit is associated with facial wasting and should be avoided, if at all possible, for this reason alone.

Doctor

d4T has potency in a range similar to that of AZT, though its long-term toxicity profile has proven to be considerably more difficult to manage. Peripheral neuropathy and elevations of serum lactate levels are seen with moderate frequency in several studies using d4T among treatment naïve patients. Fat loss, in the face and extremities, has been linked to this agent in several cohort studies as well. These events are felt likely due to disruption of cellular energy production (mitochrondial function). An extended release formulation of d4T has been approved by the FDA, but has not been released as of this writing. Studies of the extended release (XR) formulation suggest a decrease in the above mentioned toxicities when compared to the conventional form of the drug. The eventual place of d4T, given its inherent potency and toxicity remains to be determined.

—Stephen L. Becker, MD

Activist

Zerit (d4T) remains one of the more popular drugs used as part of a HIV regimen. d4T counts peripheral neuropathy and pancreatitis as its more severe side effects. There is a risk of lactic acidosis and liver toxicity in pregnant women using d4T and ddI together with Viramune. This should be monitored. Although d4T is strongly recommended in the Department of Health and Human Services (DHHS) guidelines beware, d4T has been associated with an increased risk of lipoatrophy.

—Deneen Robinson

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 one 150 mg tablet twice daily), with no food restrictions (may be taken with or without food). Dose is lower for children and people who weigh less than 110 pounds (50 kg), to 2 mg/kg (a kilogram equals 2.2 pounds). A strawberry/banana flavored liquid is also available. Take missed dose as soon as possible, but do not double up on your next 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: This remains one of the most easily tolerated medications. Potential side effects/toxicities include headache, nausea, diarrhea, fatigue, hair loss, insomnia, malaise (general ill feeling), nasal symptoms, cough, peripheral neuropathy, low white blood cells and anemia.

Rare but potentially fatal toxicity with all NRTIs is pancreatitis (inflammation of the pancreas), hepatomegaly (enlarged liver) with steatosis and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in all patients taking NRTIs but is more common and more severe in women, people who are obese and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distention, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver (called hepatomegaly with steatosis). Pancreatitis can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting and blood in the urine. Your physician will check for pancreatitis by checking for increased levels of amylase and lipase in the blood. Risks for pancreatitis include: higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Children should be monitored carefully for pancreatitis.

Potential drug interactions: No significant drug interactions.
Tips: Is also approved for treatment of hepatitis B virus (HBV), under the brand name Epivir HBV. So if you have hepatitis B and HIV, this drug works for both diseases, but make sure you are taking Epivir at HIV doses—always ask your doctor or pharmacist. 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

3TC ushered in the modern era of NRTIs. Nearly 50% more potent than the agents that preceded it, 3TC has a very favorable toxicity profile and is extremely well tolerated. The Achilles heel of 3TC is its low genetic barrier, meaning that a single mutation (M184V), disables the drug. The Federal Guidelines for the treatment of HIV includes 3TC for initial therapy whether used with PI or NNRTI-based HAART. While no resistance mutation is good, the M184V has been found to impair viral fitness, making the virus "less capable" in infecting new cells. For this reason 3TC is often maintained in regimens even after the M184V mutation appears. 3TC has been approved for once daily dosing.

—Stephen L. Becker, MD

Activist

One of the least complicated nucleoside reverse transcriptase inhibitors, 3TC is a very popular drug because of its limited side effect profile, and is strongly recommended in the Department of Health and Human Services (DHHS) guidelines. However, users beware, 3TC is also known for its quick development of the M184V mutation. Hair loss is also a side effect reported to be a side effect caused by using 3TC. 3TC has been successfully combined with AZT in the single pill formulation, Combivir; and combined with AZT and Ziagen in the single pill formulation, Trizivir. Finally, 3TC has been approved for the treatment of hepatitis B. For the dual diagnosed person, one less pill is quite appealing.

—Deneen Robinson

2x

Brand Name: Ziagen

Common Name: abacavir sulfate (ABC)

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). Once-a-day dosing submitted for FDA approval. A strawberry/banana flavored liquid is available. Take missed dose as soon as possible, but do not double up on your next dose.
Manufacturer contact: GlaxoSmithKline, www.ziagen.com, 1 (800) 722–9294
AIDS Treatment Information Service:
1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Hypersensitivity reaction (HSR, an allergic-like reaction). Approximately 5% of people (1 in 20) taking abacavir experienced hypersensitivity during clinical trials. People who think they are experiencing hypersensitivity must be evaluated by an experienced HIV provider as soon as possible before they stop taking abacavir. If treatment is stopped because of this serious reaction, they can never take abacavir or Trizivir again (called "re-challenging") because of life-threatening and in a few instances fatal reaction. (This does not apply to missed doses, when there's no HSR.) This hypersensitivity usually occurs during the second week of treatment, but may take as long as six weeks to appear, gets progressively worse and resolves quickly (24–48 hours) after permanent discontinuation. Symptoms usually, but not always, include some combination of sudden fever, muscle ache, severe nausea, vomiting or abdominal pain, severe tiredness, respiratory symptoms (cough, difficulty breathing and sore throat) and possibly mild rash. These symptoms are listed on the patient information sheet and warning card that you receive each time you fill your Ziagen prescription. You should always keep the warning card with you. 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, contact your healthcare provider immediately.

More common 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 is pancreatitis (inflammation of the pancreas), hepatomegaly (enlarged liver) with steatosis and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in all patients taking NRTIs but is more severe in women, especially with those who are overweight; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distention, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver (called hepatomegaly with steatosis). Pancreatitis can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting and blood in the urine. Your physician will check for pancreatitis by checking for increased levels of amylase and lipase in the blood. Risks for pancreatitis include: higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Children should be monitored carefully for pancreatitis.

Potential drug interactions: Avoid alcohol ingestion. Alcohol increases abacavir levels and might increase its side effects. No clinically significant interactions between abacavir and other drugs have been observed.

Tips: Studies show that abacavir crosses the blood-brain barrier to a useful degree, which may be beneficial for patients at risk for neurological damage (such as dementia) from HIV. 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.

Submitted to the FDA for approval of once-a-day dosing. An analysis of 8,000 patients found a reduced risk of HSR in blacks and in men.

Doctor

Abacavir (ABC) like 3TC and FTC is a potent agent. Unlike these agents, ABC has excellent penetration into the brain and other nervous system tissues. This is an important feature as HIV infects many cells within the central nervous system. ABC has a high genetic barrier to resistance. It therefore requires several mutations before the drug loses activity. ABC is generaly well tolerated and is not associated with major adverse events. Approximately 5% of the population has a genetic tendency to develop the so-called hypersensitivity reaction. This reaction is not an allergy, but rather a reaction permitted by a specific genetic composition. It occurs more frequently among whites and females. (For a full description, see above). Given ABC's potency and tolerability many patients will benefit from this agent as part of their initial or subsequent regimens. ABC is under study, and will likely receive approval, for once daily dosing.

—Stephen L. Becker, MD

Activist

Boy this drug can pack a punch—its hypersensitivity reaction. The hypersensitivity reaction does not allow for future Ziagen use. The manufacturer says the reaction will most likely occur during the first eleven days. In rare cases, it has occurred as many as eight months after starting. There is a warning card that comes with this product—you should carry it at all times. If you experience hypersensitivity reaction, taking this drug again can mean death. If you experience hypersensitivity, tell your physician to boldly mark your chart so that no one ever risks giving this drug to you again. Ziagen was originally marketed as an alternative to NNRTIs and protease inhibitors in a triple drug regimen but the clinical data has not supported this notion. For the newly infected and treatment naïve, it may be a good choice but for the treatment-experienced person, a triple nuke regimen may not be a good idea.

—Deneen Robinson

Brand Name: Combivir

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One tablet (150 mg lamivudine, 3TC, Epivir, 300 mg zidovudine, AZT, Retrovir), twice-a-day, with no food restrictions (may be taken with or without food). Take missed dose as soon as possible, but do not double up on your next 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: May be taken with food to decrease potential nausea associated with AZT. See drug pages for lamivudine, 3TC (Epivir) and zidovudine, AZT (Retrovir) for more details.

Potential drug interactions: See lamivudine, 3TC (Epivir) and zidovudine, AZT (Retrovir). Do not take Retrovir or Epivir while taking Combivir since these medications are already in Combivir.

Tips: Combivir is the combination of lamivudine, 3TC (Epivir) and zidovudine, AZT (Retrovir) into one pill; see the pages of those individual drugs for more information.

Doctor

See Retrovir and Epivir drug pages.
—Stephen L. Becker, MD

Activist

The first co-formulated drug, GlaxoSmithKline helped advance the simplicity in dosing HIV medications while also finding a way to keep hold of its place in the market. Bravo, GSK—it would be great if this drug were priced cheaper since it's so commonly used by ADAP formularies. Also see Retrovir (AZT) and Epivir (3TC).
—Deneen Robinson

2x

Brand Name: Trizivir

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One tablet (300 mg abacavir/Ziagen, 150 mg lamivudine, 3TC/Epivir and 300 mg zidovudine, AZT/Retrovir), twice-a-day, no food restrictions (may be taken with or without food). Take missed dose as soon as possible, but do not double up on your next 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: The most common side effects of Trizivir are the same as lamivudine, 3TC (Epivir); zidovudine, AZT (Retrovir); and abacavir (Ziagen). See those pages for more information. Side effects associated with Trizivir include headache, nausea, upset stomach, and fatigue. May be taken with food to decrease potential nausea associated with AZT. The hypersensitivity reaction (HSR, an allergic-like reaction) warning on abacavir (Ziagen) bears repeating here. Approximately 5% of people (1 in 20) taking abacavir experienced hypersensitivity during clinical trials. People who think they are experiencing hypersensitivity must be evaluated by an experienced HIV provider as soon as possible before they stop taking abacavir. If treatment is stopped because of this serious reaction, they can never take abacavir or Trizivir again (called "re-challenging") because of life-threatening and in a few instances fatal reaction. (This does not apply to missed doses, when there's no HSR.) This hypersensitivity usually occurs during the second week of treatment, but may take as long as six weeks to appear, gets progressively worse and resolves quickly (24–48 hours) after permanent discontinuation. Symptoms usually, but not always, include some combination of sudden fever, muscle ache, severe nausea, vomiting or abdominal pain, severe tiredness, respiratory symptoms (cough, difficulty breathing and sore throat) and possibly mild rash. These symptoms are listed on the patient information sheet and warning card that you receive each time you fill your Ziagen prescription. You should always keep the warning card with you. 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, contact your healthcare provider immediately.

Potential drug interactions: See also lamivudine, 3TC (Epivir) and zidovudine, AZT (Retrovir) for more information. Do not take Retrovir, Epivir or Ziagen while taking Trizivir since these medications are already in Trizivir. If you are taking one of the following medications, consult your doctor or pharmacist before starting Trizivir: stavudine, zalcitabine, ribavirin, interferon, rifabutin, rifampin, probenecid, methadone, ganciclovir, clarithromycin, pyramethamine, flucytosine, amphotericin B and hydroxyurea.

Tips: Trizivir's biggest advantage has been that it is a complete triple anti-HIV regimen in one pill. Using Trizivir by itself preserves other classes (NNRTIs and PIs) and may minimize resistance and drug interactions. The 2003 Department of Health and Human Services (DHHS) guidelines no longer recommend Trizivir as an alternative initial regimen for individuals with viral loads under 100,000 copies. Recent data has demonstrated that Trizivir and other triple nuke regimens are not as effective as NNRTI and PI containing regimens regardless of viral loads. Trizivir's use may be moving away from single therapy to combination therapy with a non-nuke or protease inhibitor.

Trizivir is the combination of abacavir (Ziagen); lamivudine, 3TC (Epivir); and zidovudine, AZT (Retrovir) into one pill; see the pages of those individual drugs for more information. An analysis of 8,000 patients found a reduced risk of HSR (from the Ziagen) in blacks and in men.

Doctor

See Retrovir, Epivir and Ziagen drug pages.
—Stephen L. Becker, MD

Activist

Trizivir is the combination of three nucleoside reverse transcriptase inhibitors. Recently there have been discussions on the efficacy of Trizivir. The Department of Health and Human Services (DHHS) guidelines suggest that Trizivir should ONLY be used as a first line regimen "when an NNRTI-based or a PI-based regimen cannot or should not be used as initial therapy." The guidelines also state that Trizivir could be used in combination with other drugs from the NNRTI or Protease Inhibitor class. For the treatment-experienced patient, this drug should not be considered, except in combination with other drugs. Trizivir is not recommended for people who weigh less that 40 kg. It is important to never start Trizivir if you have experienced the hypersensitivity reaction to Ziagen. Also see Retrovir (AZT), Epivir (3TC) and Ziagen.
—Deneen Robinson

1x

Brand Name: Emtriva

Common Name: emtricitabine, FTC

Class: nucleoside analog (also called nucleoside reverse transcriptase inhibitor, NRTI or nuke)
Standard dose: One 200 mg capsule once-a-day, with no food restrictions (may be taken with or without food). The dosing frequency needs to be adjusted for people who have decreased kidney function. Take missed dose as soon as possible, but do not double up on your next dose.
Manufacturer contact: Gilead Sciences, www.gilead.com, 1 (800) GILEAD5 (445–3235)
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Most common side effects include headache, diarrhea, nausea and rash. Peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet) may go away once Emtriva is stopped, but can be painful and permanently debilitating if not treated in time. Skin discoloration observed as a darkening of the skin on the palms and the soles of the feet can occur and usually does not cause any symptoms. Rare but potentially fatal toxicity with all NRTIs is pancreatitis (inflammation of the pancreas), hepatomegaly (enlarged liver) with steatosis and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in all patients taking NRTIs but is more common and more severe in women, people who are obese and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distention, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver (called hepatomegaly with steatosis). Pancreatitis can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting and blood in the urine. Your physician will check for pancreatitis by checking for increased levels of amylase and lipase in the blood. Risks for pancreatitis include: higher than recommended doses of NRTIs, advanced HIV, and alcohol use. Children should be monitored carefully for pancreatitis.

Potential drug interactions: No significant drug interactions observed in clinical trials.

Tips: Emtriva (FTC) is called a "me-too" drug because of its similarity to Epivir (3TC); both drugs are associated with the M184V mutation (which suggests drug resistance). However, Emtriva remains in blood cells in excess of the 24-hour dosing interval. The steady state intracellular mean half-life of the active drug is 39 hours.

Cross-resistance can occur with Epivir (3TC) and Hivid (ddC) making them less likely to work if the HIV is resistant to Emtriva. Emtriva has demonstrated efficacy against HBV but is not currently approved to treat HBV. Worsening of hepatitis B (HBV) in patients co-infected with HIV/HBV has occurred when Emtriva was discontinued. Patients co-infected with HIV/HBV who stop taking Emtriva should be closely followed by their physician. Gilead is currently working on a co-formulation of Viread (tenofovir DF) and Emtriva that would include both medications in one pill and is hoping to have this product available in 2005.

Doctor

Emtricitabine (FTC) is a drug nearly identical in all important clinical aspects to 3TC. At this time there is no apparent advantage to using either of these agents in preference to the other. FTC will soon be usefully combined with tenofovir in a single, once daily tablet.

—Stephen L. Becker, MD

Activist

The newest nuke, FTC is similar to 3TC. Gilead says it is more efficacious than 3TC, meaning it stays in the body longer. Gilead has trials going on currently looking to combine FTC with Viread (tenofovir), in a single pill formulation. It is due to market sometime in 2005. It will be the only once daily combination drug. FTC is also able to treat hepatitis B. Time will tell if this drug will have any greater benefit to HIV-positive people.

—Deneen Robinson

1x

Brand Name: Viread

Common Name: tenofovir disoproxil fumarate (TDF)

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, with no food restrictions (with or without food). Take missed dose as soon as possible, but do not double up on your next dose.
Manufacturer contact: Gilead Sciences, Inc., www.viread.com, 1 (800) GILEAD5 (445–3235)
AIDS Treatment Information Service:
1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Overall, fairly well tolerated, however, individuals may experience the following: nausea, headache, diarrhea, vomiting, asthenia, flatulence, abdominal pain and anorexia. Rare but potentially fatal toxicity with all NRTIs is pancreatitis (inflammation of the pancreas), hepatomegaly (enlarged liver) with steatosis and lactic acidosis (accumulation of lactate in the blood and abnormal acid-base balance). Lactic acidosis has been seen in all patients taking NRTIs but is more common and more severe in women, people who are obese and people who have been taking nukes for a long time; and more common in people with liver disease, but can occur in people without a history of liver damage. People with lactic acidosis may experience persistent fatigue, abdominal pain or distention, nausea/vomiting, and difficulty breathing or shortness of breath; and enlarged, fatty liver (called hepatomegaly with steatosis). Pancreatitis can be life-threatening and may cause pain in the stomach and back, along with nausea, vomiting and blood in the urine. Your physician will check for pancreatitis by checking for increased levels of amylase and lipase in the blood. Risks for pancreatitis include: higher than recommended doses of NRTIs, advanced HIV, and alcohol use.

The effect of tenofovir on children and individuals with severe hepatic (liver) 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 levels of Videx EC and Videx (ddI) are increased by 50% when given at the same time as Viread. Therefore, a dose reduction to 250 mg for Videx is recommended. The levels of atazanavir (Reyataz) are decreased by 40% when used at the same time as Viread. It remains uncertain how to overcome this interaction, though some clinicians have felt the the dose of atazanavir should be adjusted to 300 mg and boosted with 100 mg of ritonavir (Norvir), and still dosed once-a-day. This dose combination has been studied.

Tips: To its credit, Viread is successful in showing viral load decrease in people with nuke resistance and after three years of follow up studies, it continues to demonstrate good results in the growing number of people whose current triple-class therapy is failing. The body clears 70–80% of Viread through the kidney and dosing adjustment is recommended for those with impaired kidney function. Serious kidney problems have been rare and the majority has been in those with pre-existing kidney disease or receiving nephrotoxic agents. However, the manufacturer recommends that individuals with impaired kidney function be monitored closely, especially in people with advanced HIV disease, even in people who did not start out with kidney disease. Kidney function should be monitored closely, especially in people with advanced HIV disease, even in people who did not start out with kidney disease. 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. In clinical trials reduced response to Viread was associated with multiple TAMs (thymidine analog mutations), specifically the M41L or L210W. Viread selects for the K65R muation (as does abacavir and didanosine), it was seen in 3% of the Viread treatment-naive patients at two years. AZT and d4T maintain full activity and varying rates of sensitivity are seen with abacavir, tenofovir and didanosine. Further research needs to be done in this area. A co-formulation of Viread and Emtriva (FTC) may be available in 2005.

Doctor

Tenofovir (TDF) is a potent and well tolerated once daily NRTI. It has a high genetic barrier and has therefore found wide use in both treatment naïve and experienced patients. The safety and tolerability of TDF has so far been excellent, although the drug can cause kidney dysfunction in those with impaired renal function. Dosage modification is necessary for these patients. Certain drug interactions have been noted since the approval of TDF. These include ddI (see above) and the protease inhibitor atazanavir (see that drug page). The mechanism of these interactions is currently under study and other drug—drug interactions are possible. As noted previously, tenofovir will be combined with FTC in a single, once daily tablet.

—Stephen L. Becker, MD

Activist

One of the few drugs excreted through the kidneys, tenofovir has successfully demonstrated it works well against HIV and hepatitis B. Gilead is following in the steps of GlaxoSmithKline and looking to combine this drug with Emtriva (FTC) in a single pill formulation by 2005. So we'll have another once daily option. Proceed cautiously if you have a history of kidney problems. Also caution is recommended when tenofovir is used with other drugs known for renal toxicity. Although no major side effects were reported, tenofovir must be taken with food; if not you may experience nausea.

—Deneen Robinson

Brand Name: Rescriptor

Common Name: delavirdine (DLV)

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke)
Standard dose: One 400 mg tablet three times a day (or two 200 mg tablets or four 100 mg tablets three times a day). Only the 100 mg tablets can be dissolved in liquid, however avoid grapefruit juice; no food restrictions (may be taken with or without food). Take missed dose as soon as possible, but do not double up on your next dose.
Manufacturer contact: Agouron Pharmaceuticals, a Pfizer company, www.agouron.com, 1 (888) 777–6637
AIDS Treatment Information Service:
1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Most common side effects include headache, nausea, vomiting, diarrhea, fatigue, elevated liver enzymes, itchy skin or rash. A serious side effect of the NNRTI class is rash, which can be life-threatening. If you experience blistering, mouth lesions, conjunctivitis (redness or inflammation of eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever or general malaise (general ill feeling), stop taking Rescriptor and seek immediate medical attention.

Potential drug interactions: You cannot take the following medications with Rescriptor: Versed (midazolam), Halcion (triazolam) and Xanax (alprazolam), pimozide (a psychiatric medication), ergot alkaloids (Wigraine and Cafergot) in any form—serious interactions are seen with dilation during gynecological exams. Do not use Zocor (simvastatin) or Mevacor (lovastatin) cholesterol (lipid) lowering meds; suggested alternatives are Lipitor (atorvastatin), Lescol (fluvastatin), and Pravachol (pravastatin, the one that looks best on paper for people on protease inhibitors). Liver enzymes should be checked regularly if you are on these cholesterol meds, as they can increase risk for liver toxicity with Rescriptor. Certain amphetamines and antiarrhythmic drugs should not be used with Rescriptor, therefore inform your healthcare provider if you have a history of heart or blood pressure problems. Potential toxicity when given with Biaxin (clarithromycin), dapsone, Mycobutin (rifabutin), Procardia (nitedipine), Coumadin (warfarin) and quinidine. Tegretol (carbamazepine, an anti-seizure medication used to treat peripheral neuropathy), phenobarbital, Dilantin (phenytoin), Mycobutin (rifabutin) and rifampin (used to treat tuberculosis) are drugs that decrease Rescriptor levels. Rescriptor increases levels of Crixivan, Fortovase, Invirase, Kaletra, Reyataz and methadone.

Tips: Research demonstrates smaller doses of Rescriptor increases blood levels of some protease inhibitors, making it unique among the NNRTIs. Videx (not Videx EC), antacids (like Tagamet, Zantac and Tums) and gastric achlorhydria (low stomach acid) decreases absorption of Rescriptor, so take at least one hour apart from these drugs and with acidic beverages such as orange or cranberry juice. Do not use herbal preparations, such as St. John's wort, without checking with your healthcare provider or pharmacist.

Doctor

Delavirdine (DLV) is an infrequently used NNRTI. Its effectiveness appears to be less than that of either Viramune or Sustiva. Rash and hepatotoxicity are less frequent. Unless further study demonstrates a currently unappreciated advantage of DLV, there is little reason to use this agent in preference to the better studied Viramune or Sustiva.

—Stephen L. Becker, MD

Activist

The oldest and least used of the non-nukes. After all these years, the true benefit of this drug has yet to be discovered. Agouron has been looking at using delavirdine to boost nelfinavir, but the early reports indicate significant diarrhea as one of the side effects. Perhaps instead of using delavirdine to boost protease inhibitors this drug can be reformulated to give people another viable option from the non-nuke class.

—Deneen Robinson

2x

Brand Name: Viramune

Common Name: nevirapine (NVP)

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. If rash occurs in first two weeks, it is important to report condition to healthcare provider as soon as possible. No food restrictions (may be taken with or without food). Liquid formulation is available. Take missed dose as soon as possible, but do not double up on your next dose.
Manufacturer contact: Boehringer-Ingelheim, www.viramune.com, 1 (800) 274–8651
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Most common side effects include headache, nausea, vomiting and rash. The reason for the 14-day lead-in dosing is to reduce the frequency of rash. A serious side effect of the NNRTI class is rash, which can be life-threatening. If you experience blistering, mouth sores, conjunctivitis (redness or inflammation of eye, or pink eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever or general malaise (general ill feeling), stop taking Viramune and your other anti-HIV meds 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. An increase in liver enzyme levels has been observed and in rare instances the development of hepatitis. 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.

Potential drug interactions: Methadone dose may need to be increased due to withdrawal symptoms. Viramune reduces levels of protease inhibitors. If they are taken at the same time 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 not with Mycobutin (rifabutin). The effectiveness of birth control pills may be decreased when taking Viramune; women and their male partners should consider the use of alternative contraception methods with barrier.

Tips: Because of the incidence of rash (9% of any grade through 52 weeks of treatment) 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. Women may be at higher risk for rash. 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 healthcare provider. 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. In any case, let your medical provider know you have a rash. Monitor liver function tests during first six months, initially every two weeks. The increased period of risk for liver injury is primarly in the first 6–12 weeks of taking Viramune. Do not ignore yellowing of your eyes or skin, as this may be a sign of a severe liver effect.

Studies show that Viramune crosses the blood-brain barrier to a useful degree, which may be beneficial for patients at risk for neurological damage (such as dementia) from HIV. Nevirapine has also been shown to have a positive impact on cholesterol and triglycerides levels. When given around the time of labor Viramune has demonstrated effectiveness in preventing the transmission of HIV from mother to child, but there was an increase in HIV drug resistance in the moms. Single or double dose nevirapine may be used for babies born to HIV-positive mothers.

Doctor

Nevirapine (NVP) like the class of NNRTIs is an extremely potent agent with excellent penetration into the central nervous system. Like the class of agents, NVP has a low genetic barrier to resistance, a distinct toxicity profile and the ability to interact with numerous other drugs (HIV and non-HIV). NVP was recently compared with efavirenz in a large clinical trial, and found to have comparable effectiveness. Rash occurs in nearly 30% of patients, with occasional serious manifestations. Liver toxicity (hepatotoxicity) occurs in 8–15% of patients, usually within the first 6 to 12 weeks of therapy. There have been fatal cases of hepatotoxicity reported with NVP. NVP has been used extensively and effectively to prevent mother to child transmission of HIV. NVP has an unexplained beneficial effect on serum cholesterol, raising the cardio-protective HDL component.

—Stephen L. Becker, MD

Activist

The data recently released from the 2NN study suggests that Viramune is as effective as Sustiva. With the ADAP crisis, the cost of this drug makes it a viable alternative. The success of nevirapine in stopping mother-to-child transmission makes this drug a good choice for use internationally. However, it has its own problems. In addition to the common NNRTI life-threatening rash, Viramune has a black box warning for its severe liver toxicity. It has been reported to cause hepatitis. It is also reported that Hispanics and people with a history of sulfa rash are more at risk of rash when starting Viramune.

—Deneen Robinson

1x

Brand Name: Sustiva

Common Name: efavirenz (EFV)

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 3 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 up on your next 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: Because Sustiva penetrates so readily into the brain, up to 50% of patients experience some kind of central nervous system symptoms (dizziness, headache, somnolence or hypnotic trance). Psychiatric symptoms (confusion, insomnia, hallucinations, vivid dreams or nightmares, depression, euphoria or mania, agitation) are less frequent. Some people in recovery from substance use will experience flashbacks. Other side effects include rash, nausea, vomiting, diarrhea, fever, insomnia and increased liver enzymes. These symptoms occur early and generaly resolve within two to four weeks. A serious side effect of the NNRTI class is rash, which can be life-threatening. If you experience blistering, mouth lesions, conjunctivitis (redness or inflammation of eye, which if untreated may result in permanent vision loss), swelling, muscle or joint aches, fever or general malaise (general ill feeling), stop taking Sustiva and seek immediate medical attention. Rash is more common, and more severe, in children, as is diarrhea, fever and low levels of some blood cells. May raise levels of triglycerides and the good cholesterol (HDL). May lead to false positive tests for use of marijuana. Women taking Sustiva should not become pregnant or breast-feed because of the risk of birth defects.

Potential drug interactions: You cannot take the following medications with Sustiva: Versed (midazolam), Halcion (triazolam), or ergot medications (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. Dosing adjustment may be necessary for people on methadone due to withdrawal symptoms. When taken with Sustiva, Crixivan should be increased to 1,000 mg every eight hours and Kaletra to four capsules twice daily. Reyataz should be "boosted" with Norvir (Reyataz 300 mg/Norvir 100 mg), still once daily, when taken with Sustiva. 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. Monitor liver enzymes closely if Sustiva and Norvir are used together due to potential risk of liver damage.

Tips: Women of child-bearing age and their male partners should consider the use of alternative contraception methods with barrier, in addition to the Pill, because of the potential for embryo heart defects. It is recommended that Sustiva be taken at bedtime to help reduce CNS symptoms, but can be taken at any time. People have described having "happy dreams" or nightmares depending on their mood or types of movies (horror movie or Disney movies, for example) or television shows they viewed before sleep. Avoid driving or operating heavy machinery for a few hours after dose. Side effects may linger. Taking Sustiva with high-fat food, as well as alcohol, may increase the concentration of Sustiva and the risk of experiencing side effects. Some people adjust to Sustiva when taking Ativan or Ambien to sleep for the first few weeks, but either may make you even more groggy the next morning. Shown to penetrate lymphoid tissue, a hiding place for HIV.

Doctor

Efavirenz (EFV) is an extremely potent agent, and like NVP has excellent central nervous system penetration. Like the other agents in this class, EFV too has a low genetic barrier to resistance and a distinct toxicity profile. Likely because of its penetration into the nervous system, the most frequent toxicity associated with EFV is related to mood and affect. Nearly 50% of patients experience some form of nervous system side effects, though the vast majority are mild, and resolve over time. Rash and hepatotoxicity are less common than with NVP. EFV cannot be used in pregnant women. EFV in combination with two NRTIs (ZDV + 3TC, d4T + 3TC or TDF + 3TC) is listed as a preferred regimen in Federal guidelines. These recommendations come from the demonstrated effectiveness of EFV-containing regimens in several large clinical trials. EFV is the only NNRTI with this recommendation.

—Stephen L. Becker, MD

Activist

Sustiva is a powerful drug and for those people who can take it—it works. It has gained strongly recommended status for treatment of naïve patients in the Department of Health and Human Services (DHHS) guidelines. While it is one of the more commonly prescribed drugs, due in part to its once daily dosing, it has some potentially severe central nervous system (CNS) side effects. Everyone, especially people with histories of addiction, psychiatric symptoms or suicidal ideations, should be warned of the potential severity of its side effects.

—Deneen Robinson

Photo not available due to experimental status

2x

Brand Name: Not yet established

Common Name: capravirine

Class: non-nucleoside analog (also called non-nucleoside reverse transcriptase inhibitor, NNRTI or non-nuke). Capravirine shows *in vitro* activity against most virus which are resistant to the other members of the class. Capravirine is currently in Phase II/III clinical trials and patients are being actively recruited by more that 60 research centers in the United States and Canada.
Standard dose: To be determined. Studies are in progress with twice-a-day doses varying between 200 and 1400 mg. Should be taken with meals
Sponsor contact: Agouron Pharmaceuticals, a Pfizer company, 1 (888) 777–6637
AIDS Clinical Trials Information Service:
1 (800) TRIALS–A (874–2572)

Potential side effects and toxicity: The most common side effects reported in clinical trials are headache, diarrhea, nausea and vomiting.

Potential drug interactions: Capravirine is primarily metabolized by the CYP 3A4 enzyme. Other drugs metabolized by or altering the activity of this enzyme may affect blood levels of capravirine. Capravirine may also affect the blood levels of these drugs. Final dosing recommendations are being evaluated.

Tips: Capravirine is much better tolerated and absorbed when taken with food. There are no differences between low fat and high fat meals.

Doctor

The first of the "second generation" NNRTIs, with activity against the most common resistant viral variants, including those containing the signature K103N mutation. Capravirine is reasonably well tolerated, though in animal studies inflammation of blood vessels was noted. This has not been seen in human subjects enrolled in the current phase of studies. It is unclear at this time how effective capravirine will prove to be. It is clear that agents capable of salvaging first generation NNRTI failures are needed.

—Stephen L. Becker, MD

Activist

Statement not provided.

3x

Brand Name: Invirase

Common Name: saquinavir hard-gel (SQV-HGC)

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 + Norvir 100 mg once daily or Invirase 1000 mg + Norvir 100 mg twice-a-day. Take a missed dose as soon as possible, but do not double up on your dose.
Manufacturer contact: Roche Pharmaceuticals, www.rocheusa.com, 1 (800) 910–4687
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Most common are stomach related: diarrhea, abdominal discomfort and nausea. Because there is low absorption (4 to 6%) of the drug into the body, there are few other side effects. As seen with all other protease inhibitors are increased levels of cholesterol and triglycerides, except possibly unboosted Reyataz (atazanavir) and these increased levels may be associated with heart disease. Other possible side effects are 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 take with Tambocor (flecainide), Rythmol (propafenone), Versed, Halcion, Hismanol, Seldane, rifampin, ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form—serious interactions seen with dilation during gynecological exams), garlic supplements, or the herb St. John's wort. Do not use Zocor (simvastatin) or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastain), Lescol, and Pravachol (parvastatin), but they should be used with caution due to potential for liver toxicity.

Viramune, Sustiva and Mycobutin (rifabutin) decreases Invirase levels. Invirase may increase dapsone levels. Antifungal Nizoral (ketoconazole) or Sporonox (itraconazole), used for treatment of candidiasis (thrush), increases the amount of Invirase in the body. 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 concentrations.

Protease inhibitors increase blood levels of Viagra (sidenafil citrate), so initially the Viagra dose should be 12.5 mg (¼ of 50 mg tablet) and increased as needed and tolerated. It's recommended that people on PIs do not exceed 25 mg of Viagra in a 48-hour period because of potential for serious reaction.

Tips: Invirase has made a comeback, due to study results indicating strong efficacy with fewer side effects when taken with a mini-dose of Norvir, as compared to Fortovase/Norvir. This older version of saquinavir hard-gel capsules is rarely used except in combination with Norvir (low-dose) to minimize gastrointestinal adverse events. Must be taken with food. There is also some research supporting Invirase 1000 mg + Kaletra standard dose twice-a-day.

Doctor

Saquinavir was the first approved PI in 1995. Its initial hard gelatin capsule formulation was replaced by a soft gelatin capsule that improved absorption (bioavailability) but was associated with greater gastrointestinal toxicity. In the current era of ritonavir "boosted" PIs, it is now possible, and preferable to use the original hard gel capsule formulation. The combination of SQV with ritonavir can be used twice or once daily. Like fos-amprenavir (see that drug page), when used in treatment experienced patients, the twice daily regimen should be employed. Serum cholesterol and triglyceride elevations are relatively modest with this agent, and overall the drug is reasonably well tolerated. There is some suggestion that drug levels may be higher in women than men. This is being actively investigated, and at this time there are no sex-related dosing differences. Studies of SQV with Kaletra, fos-amprenavir and atazanavir are ongoing. The use of these agents in combination has appeal given complementary patterns of resistance and toxicity.

—Stephen L. Becker, MD

Activist

This was the first protease inhibitor created to treat HIV. The hard gel capsule has low boiavailability except when taken with grapefruit juice. As a result saquinavir HGC is only recommended to be taken with ritonavir. It is clear that the benefit of this drug can only be achieved when boosted. Beware: the doctor should write out the brand name due to the other formulation of saquinavir.

—Deneen Robinson

q8h

Brand Name: Crixivan

Common Name: indinavir sulfate

Class: HIV protease inhibitor (PI)
Standard dose: Rarely used by itself (two 400 mg capsules every eight hours with no food or a low-fat snack). Almost always boosted with Norvir: 400 mg Crixivan + 400 mg Norvir BID; 800 mg + 100 mg BID; or 800 mg + 200 mg BID (all combination doses taken with food). Take a missed dose as soon as possible, but do not double up on your dose. Also available in 100 mg, 200 mg and 333 mg capsules.
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: Potential side effects include: headache, fatigue or weakness, malaise (general ill feeling), nausea, diarrhea, stomach pains, loss of appetite, yellowing of skin/eyes, changed skin color, dry mouth/sore throat, taste changes, painful urination, indigestion, joint pain, hives, and liver toxicity. Itchy/dry skin, ingrown toe nails and hair loss are unique to Crixivan. Kidney stones, which may lead to more serious problems, can also occur. If pain develops in the middle to lower stomach or the back, or if there is blood in the urine call your healthcare provider immediately. Drugs such as Bactrim and Dapsone are associated with hemolytic anemia, so be careful when using indinavir. Hemolytic anemia is the fast breakdown of red blood cells. It is rare but can lead to severe problems—monitoring red blood counts is necessary. An increase in bilirubin (a test of liver function) has been reported, but it is not associated with liver problems. It may sometimes cause yellowing of the skin or eyes. As seen with all other protease inhibitors are increased levels of cholesterol and triglycerides, except possibly unboosted Reyataz (atazanavir) and these increased levels may be associated with heart disease. Other possible side effects are 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 take with Tambocor (flecainide), Rythmol (propafenone), Versed, Halcion, Hismanol, Seldane, rifampin, pimozide (a psychiatric drug), ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form—serious interactions seen with dilation during gynecological exams), garlic supplements, or the herb St. John's wort. Do not use Zocor (simvastatin) or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastain), Lescol, and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity.

Increase Crixivan to 1,000 mg every eight hours when taken with Viramune or Sustiva. Reduce Crixivan to 600 mg every eight hours when taken with Rescriptor. Reduce Crixivan to 600 mg every eight hours when taken with Sporanax (itraconazole, 200 mg twice-a-day) or Nizoral (ketoconazole, 200 mg once-a-day) or ketoconazole.

The dose of rifampin (Mycobutin) should be reduced by 50% and increase Crixivan dose to 1000 mg every eight hours when taken together.

Protease inhibitors increase blood levels of Viagra (sidenafil citrate), so initially the Viagra dose should be 12.5 mg (¼ of 50 mg tablet) and increased as needed and tolerated. It's recommended that people on PIs do not exceed 25 mg of Viagra in a 48-hour period because of potential for serious reaction.

Tips: Combining PIs continues to be a common practice today—some combinations with lower doses of Crixivan include: Crixivan 1200 mg with 1250 Viracept each twice-a-day; and Crixivan 600 mg with standard dose of Kaletra each twice-a-day. It is recommended that you drink at least 48 oz fluids daily, preferably water or clear liquids (soda pop doesn't count!) to decrease the chances of a kidney stone forming. Large amounts of coffee or alcohol can increase risk of stones. Stones may continue after stopping Crixivan. Grapefruit juice decreases Crixivan blood levels. Should be stored in original container and kept dry.

Doctor

Indinavir, a stalwart of the PI class, has found less use as newer agents have emerged. The main reason for this has been, for many, the long-term toxicity of the agent. IDV initially required dosing three times per day, on an empty stomach. When "boosted" with ritonavir, IDV can be dosed twice daily without regard to meals. Unfortunately, in the doses studied and most commonly used, the levels of IDV are increased to an extent that side effects are even more common in the boosted combinations. Despite its proven effectiveness, until an optimum dose combination is found, favorably balancing effectiveness and toxicity, other PIs appear as more attractive options.

—Stephen L. Becker, MD

Activist

Although saquinavir-HGC was the first protease inhibitor, Crixivan revolutionized the treatment of HIV disease. Crixivan was labeled "the cure". In combination, it gave us hope, undetectable viral loads and the "crix" belly. Crixivan is to be taken three times daily due to its short half-life. Now "Crix" can be boosted with Norvir (ritonavir) and taken twice daily. You must drink lots of water or you may develop kidney stones. Women may get the "crix" sludge around their organs. The drawback to being the first is the list of side effects that are now associated with protease inhibitors such as lipodystrophy, diabetes and elevated lipids. The strict schedule of three times daily along with food and water requirements requires some discipline. If your life is busy ask for the boosted version. Too many missed doses and you will develop resistance; not just to Crixivan but other PIs as well.

—Deneen Robinson

Brand Name: Norvir

Common Name: ritonavir

Class: HIV protease inhibitor (PI)
Standard dose: Almost never used at its approved dose (a lead-in dosing, then six 100 mg soft gelatin capsules twice-a-day, preferably with food—dose escalation is important to avoid side effects). Norvir is primarily used as a boosting agent for other PIs. Take a missed dose as soon as possible, but do not double up on your dose. Approved for children ages 2 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)

Potential side effects and toxicity: Most common side effects include: weakness, stomach pain, upset stomach (nausea, diarrhea, and vomiting), tingling/numbness around the mouth, hands or feet, loss of appetite, taste disturbance, weight loss, headache, dizziness, pancreatitis (see nukes), and alcohol intolerance.

As seen with all other protease inhibitors are increased levels of cholesterol and triglycerides, except possibly unboosted Reyataz (atazanavir) and these increased levels may be associated with heart disease. Other possible side effects are 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.

Other potential side effects are liver problems, such as increase in liver enzymes (AST, ALT and GGT), hepatitis, or jaundice (yellowing of skin); and increased muscle enzyme (CPK) and uric acid. People with hepatitis B or C may be at increased risk.

Potential drug interactions: Ritonavir interacts with many other drugs. See the package insert for the most complete list. Do not take with Tambocor (flecainide), Rythmol (propafenone), Versed, Halcion, Hismanol, Seldane, rifampin, ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form—serious interactions seen with dilation during gynecological exams), Antabuse or Flagyl, garlic supplements, or the herb St. John's wort. Do not use Zocor (simvastatin) or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastatin), Lescol, and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity.

Protease inhibitors increase blood levels of Viagra (sidenafil citrate), so initially the Viagra dose should be 12.5 mg (¼ of 50 mg tablet) and increased as needed and tolerated. It's recommended that people on PIs do not exceed 25 mg of Viagra in a 48-hour period because of potential for serious reaction.

Levels of the street drug Ecstasy are 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.

Tips: The real strength of Norvir is in combination with other PIs (used as a boosting agent), allowing for a lower dose of both. Stomach side effects are reduced by taking Norvir with high fat foods (such as peanut butter or avocado)—however be careful because some other HIV medicines should not be taken with high fat foods. You can mix liquid solution in ice cream, milk or pudding to hide the bitter taste. Capsules do not need refrigeration if stored below 77° F and used within 30 days, but keep them in original container. The capsules contain castor oil and have bitter taste. Chocolate masks the bitter taste. Plasma concentration increases in people with hepatic (liver) impairment.

Doctor

Ritonavir is no longer used as a sole PI, but rather as a means of "boosting" other PIs. When used as a sole PI, the doses were associated with undue toxicity and intolerance. The doses used for "boosting" are, for the majority, well tolerated. Given the inherent limitations of PIs, the need for ritonavir in its "boosting" capacity will remain in the foreseeable future.

—Stephen L. Becker, MD

Activist

Norvir is a very potent protease inhibitor. It was FDA approved faster than any drug to date. However, this drug is better known for its horrible taste, ability to cause numbness of the mouth and tongue and the astounding number of contraindications. The best use of Norvir has been in giving children a potent protease inhibitor and its enhancement of other protease inhibitors. When Norvir is used as a booster, the side effects including the contraindications are lessened. Perhaps this is the best way to go with this drug unless you do not have any other choices.

—Deneen Robinson

3x

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 twice-a-day with food. (Two 625 mg tablets approved by FDA, but not yet available.). Take a missed dose as soon as possible, but do not double up on your dose. Viracept Oral Powder also available for children and individuals unable to swallow tablets.
Manufacturer contact: Agouron Pharamaceuticals, a Pfizer company, www.viracept.com, 1 (888) 777–6637
AIDS Treatment Information Service:
1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Most common include: diarrhea (15-20% of patients in Study 542), stomach discomfort, nausea, gas, weakness and rash.

As seen with all other protease inhibitors are increased levels of cholesterol and triglycerides, except possibly unboosted Reyataz (atazanavir) and these increased levels may be associated with heart disease. Other possible side effects are 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 other drugs in this class.

Do not take with Tambocor (flecainide), Rythmol (propafenone), Versed, Cordarone (amiodarone), Halcion, Hismanol, Seldane, rifampin, ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form—serious interactions seen with dilation during gynecological exams), garlic supplements, or the herb St. John's wort. Do not use Zocor (simvastatin) or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastain), Lescol, and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity. Rifampin and Viracept should not be used together.

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). Mycobutin (rifabutin) dose must be decreased when used with Viracept. Prescriber may need to adjust doses of any of these drugs accordingly.

Protease inhibitors increase blood levels of Viagra (sidenafil citrate), so initially the Viagra dose should be 12.5 mg (¼ of 50 mg tablet) and increased as needed and tolerated. It's recommended that people on PIs do not exceed 25 mg of Viagra in a 48-hour period because of potential for serious reaction.

The effectiveness of birth control pills may be decreased when taking Viracept; women and their male partners should consider the use of alternative contraception methods with barrier.

Tips: Viracept tablets have a film coating that prevents them from dissolving while swallowing. Do not leave pharmacy without anti-diarrhea meds such as Immodium, Tums or other calcium products. Also try Solgar oat bran tablets, psyllium husk fiber bars and pancreatic enzymes (all with meals). As an extra precaution, take a change of clothes with you everyday for the first several weeks—stick it out, most often symptoms improve after two or three weeks. The Oral Powder tastes horrible and requires a large amount for mixing into food. Patients can crush adult tablets for use in children or dissolve tablets in a small amount of water. Acidic food or juice (e.g. orange/apple juice or apple sauce) not recommended in combination with Viracept, due to resulting bitter taste. To get the full benefit of Viracept, it must be taken with a meal of at least 500 calories, with at least 20% to 50% of those calories coming from fat. Examples of meals that help to get to adequate food intakes include: Taco Bell Breakfast Burrito and 8 oz of Non-Acid Juice (650 calories, 35% from fat) or Subway Tuna Sandwich including potato chips and 8 oz of skim milk (703 calories, 41% from fat).

Doctor

Nelfinavir, at one time the most frequently used PI, and despite a novel pattern of resistance development, has lost the favor of its earlier years. NFV, among the PIs is probably most highly dependent on a full stomach for adequacy of absorption. In addition, the percentage of fat in the meal greatly affects NFV absorption. As a result, the effectiveness of this agent is clinically diminished in any but a high fat, high calorie meal. This may underlie the relatively poor performance of NFV when tested against other PIs in clinical trials. NFV use may also be limited by diarrhea, and elevated serum cholesterol and triglycerides in some. NFV, because of its metabolism, has not benefited from ritonavir "boosting". NFV is often used in pregnant women. Nelfinavir drug level determinations are essential in this patient population.

—Stephen L. Becker, MD

Activist

Diarrhea has plagued this popular drug since it was released to market. The manufacturer, Agouron, has done an excellent job of educating clients and offering physician's prescription and over-the-counter options to eliminate diarrhea. This side effect can be exacerbated by the food you eat. Interestingly, the manufacturer states that Viracept is boosted by fat in the diet. To get the best use up to 50 grams of fat is recommended in each meal at time of taking medications (breakfast and dinner). They should list weight gain as a side effect because that is inevitable with that much fat in your daily diet. Beware simple gas can turn into diarrhea. Despite these issues, Viracept is a really good potent protease inhibitor. It has demonstrated efficacy in both treatment naïve and experienced patients. It has a unique key mutation, D3ON, which saves other protease inhibitor choices. It gives you "downstream" options. However, you have to be taking the medicine when the resistance test is done for the test to be accurate.

—Deneen Robinson

Brand Name: Fortovase

Common Name: saquinavir soft-gel

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 up on your next dose.
Manfacturer contact: Roche Pharmaceuticals, www.fortovase.com, 1 (800) 910–4687
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Most common include diarrhea, nausea, stomach pain, gas, indigestion, vomiting, headaches, insomnia, fatigue, body aches, anxiety, depression and taste alteration.

As seen with all other protease inhibitors are increased levels of cholesterol and triglycerides, except possibly unboosted Reyataz (atazanavir) and these increased levels may be associated with heart disease. Other possible side effects are 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 take with Tambocor (flecainide), Rythmol (propafenone), Versed, Halcion, Hismanol, Seldane, rifampin, ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form—serious interactions seen with dilation during gynecological exams), garlic supplements, or the herb St. John's wort. Do not use Zocor (simvastatin) or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastatin), Lescol, and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity. Rifampin and Fortovase should not be used together.

Increased blood levels when taken with Crixivan, Norvir and Viracept. Blood levels are decreased significantly by Sustiva and Viramune, but can be taken together if Norvir is included. Other drugs that may also reduce Fortovase blood levels are Decadron and Tegretol, Dilantin, and phenobarbital. High incidence of liver problems, and severe ones, when taken with Rescriptor. The side effects of calcium channel blockers, clindamycin, dapsone and quinidine may be increased if taken with saquinavir.

Protease inhibitors increase blood levels of Viagra (sidenafil citrate), so initially the Viagra dose should be 12.5 mg (¼ of 50 mg tablet) and increased as needed and tolerated. It's recommended that people on PIs do not exceed 25 mg of Viagra in a 48-hour period because of potential for serious reaction.

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.

Doctor

Saquinavir was the first approved PI in 1995. Its initial hard gelatin capsule formulation was replaced by a soft gelatin capsule that improved absorption (bioavailability) but was associated with greater gastrointestinal toxicity. In the current era of ritonavir "boosted" PIs, it is now possible, and preferable to use the original hard gel capsule formulation. The combination of SQV with ritonavir can be used twice or once daily. Like fosamprenavir (see that drug page), when used in treatment experienced patients, the twice daily regimen should be employed. Serum cholesterol and triglyceride elevations are relatively modest with this agent, and overall the drug is reasonably well tolerated. There is some suggestion that drug levels may be higher in women than men. This is being actively investigated, and at this time there are no sex-related dosing differences. Studies of SQV with Kaletra, fos-amprenavir and atazanavir are ongoing. The use of these agents in combination has appeal given complementary patterns of resistance and toxicity.

—Stephen L. Becker, MD

Activist

The remake of Invirase—Fortovase is better absorbed. Food actually helps the absorption. Unfortunately, it must be taken three times a day. Further study has found that when boosted with ritonavir, Fortovase could be taken twice daily—simpler. This drug has yet to meet its full potential. The reputation of the prior formulation still lingers over Fortovase. The six pills three times a day does not help.

—Deneen Robinson

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 up on your next 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.agenerrase.com, 1 (800) 722–9294
AIDS Treatment Information Service:
1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Most common include: nausea, vomiting, stomach pain, taste disorders, fatigue, headache, mood disorders, anemia and rash. Rash occurred in about 22% of people on Agenerase, but severe rashes were uncommon. If you experience a rash, notify your doctor. For mild or moderate rashes, your doctor may choose to continue Agenerase, with close follow-up and monitoring. Because Agenerase is a sulfonamide, it should be used with caution in patients with allergies to sulfa drugs. Severe rash (see Viramune) and stomach problems (pancreatitis—see NRTIs) while rare, can be severe; notify your healthcare provider immediately.

As seen with all other protease inhibitors are increased levels of cholesterol and triglycerides, except possibly unboosted Reyataz (atazanavir) and these increased levels may be associated with heart disease. Other possible side effects are 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 take with Tambocor (flecainide), Rythmol (propafenone), Versed, Halcion, Hismanol, Seldane, rifampin, ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form—serious interactions seen with dilation during gynecological exams), garlic supplements, or the herb St. John's wort. Do not use Zocor (simvastatin) or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastatin), Lescol, and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity. Do not take extra vitamin E.

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.

Other drugs that may be involved in interactions with Agenerase include drugs for your heart (antiarrhythmics, anticoagulants, blood pressure medications, cholesterol medications), drugs for seizures, antibiotics and antifungals, sedatives, steroids, immunosuppresants, drugs for heartburn or acid reflux, oral contraceptives, and antidepressants. If you are taking any of these drugs, be sure to let your doctor and pharmacist know so they can monitor your therapy or make adjustments to your medications.

Protease inhibitors increase blood levels of Viagra (sidenafil citrate), so initially the Viagra dose should be 12.5 mg (¼ of 50 mg tablet) and increased as needed and tolerated. It's recommended that people on PIs do not exceed 25 mg of Viagra in a 48-hour period because of potential for serious reaction.

Tips: On its way to extinction due to new formulation on the market, fos-amprenavir calcium (Lexiva). If you are on Agenerase, you should talk with your doctor about switching to Lexiva. Alternative doses: Agenerase 1200 mg with Norvir 200 mg both once daily; or Agenerase 600 mg with Norvir 100 mg both twice daily. However, you should avoid taking Agenerase with food high in fat, while side effects of Norvir are reduced with food high in fat. Go figure.

May also penetrate the lymph nodes, where virus can hide out. Label warning: Agenerase Oral Solution should not be given to infants and children below the age of 4 years and should not be used by pregnant women because of the propylene glycol amount.

Doctor

Amprenavir, and the newly approved pro-drug formulation, fos-amprenavir, have been studied in both treatment naïve and treatment experienced patients. Fos-amprenavir has substantial flexibility, and can be used as a sole PI, twice daily, or boosted with ritonavir and given either once or twice daily. When used in treatment experienced patients, fos-amprenavir should be dosed twice daily with ritonavir. In clinical studies, fos-amprenavir was found to be quite effective among patients with low CD4 count and/or high viral load. Fos-amprenavir has a favorable metabolic profile compared to several other PIs, but not to the same extent as atazanavir. Amprenavir has been used successfully when combined with Kaletra, despite a drug interaction. However the combination of fos-amprenavir and Kaletra has a significantly more profound interaction, making the use of this combination contraindicated.

—Stephen L. Becker, MD

Activist

Having this drug in your regimen requires taking a lot of pills—sixteen for this product alone. With the trend towards simplified dosing, amprenavir has become more popular since it can be boosted with Norvir (ritonavir), thereby reducing the number of pills. Agenerase can be taken in an oral form as well. Asians, Eskimos, Native Americans and women may be at increased risk for toxicity from the oral solution due to their decreased ability to metabolize the propylene glycol in the oral solution. Also, it should not be taken with echinacea, St. John's wort, vitamin E, garlic and milk thistle.

—Deneen Robinson

Brand Name: Kaletra

Common Name: lopinavir/ritonavir

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 up on your next dose.
Manufacturer contact: Abbott Laboratories, www.kaletra.com, 1 (800) 222–6885
AIDS Treatment Information Service:
1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Rash, diarrhea, nausea, vomiting, stomach pain, headache, muscle weakness, increased cholesterol and triglycerides (fats in the blood), and AST/ALT (liver function tests, a sign of liver damage; this may be more common in people with hepatitis B or C).

As seen with all other protease inhibitors are increased levels of cholesterol and triglycerides, except possibly unboosted Reyataz (atazanavir) and these increased levels may be associated with heart disease. Other possible side effects are 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 take with Versed, Halcion, Hismanol, Seldane, rifampin (Rimactane, Rifadin, Rifater or Rifamate—however, recent studies show that increasing the total daily dose of Kaletra may be an option), ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form—serious interactions seen with dilation during gynecological exams), garlic supplements, or the herb St. John's wort. Do not use Zocor (simvastatin) or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastatin), Lescol, and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity. Oral solution contains alcohol, so do not use with Antabuse or Flagyl. Also avoid dihydropuridine calcium channel blockers.

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. Kaletra may lower levels of Retrovir and Ziagen. Videx should be given an hour before or two hours after Kaletra, as Kaletra should be taken with food. Mycobutin (rifabutin) dosage should be reduced to 150 mg every other day (or 150 mg three times per week) when used with Kaletra. 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. Mepron levels may be reduced with Kaletra. Avoid Sporanox doses greater than 200 mg per day with Kaletra. People with kidney impairment may require lower Biaxin doses with Kaletra. Transplant medicines like Sandimmune, Gengraf, Neoral, Prograf and Rapamune require close monitoring with Kaletra. Kaletra may alter coumadin levels. Steroids, especially Decadron, may decrease levels of Kaletra.

Protease inhibitors increase blood levels of Viagra (sidenafil citrate), so initially the Viagra dose should be 12.5 mg (¼ of 50 mg tablet) and increased as needed and tolerated. It's recommended that people on PIs do not exceed 25 mg of Viagra in a 48-hour period because of potential for serious reaction.

Tips: Doctors and patients report that this protease inhibitor is very tolerable. Great viral load results out to 5 years in people on their first HIV regimen. Good results also seen in heavily treatment-experienced adults, when compared to Reyataz, even those with protease inhibitor resistance. Use Kaletra with caution in people with mild to moderate hepatic (liver) impairment. The taste may be unappealing due to Norvir. Studies examining strength and durability of once-a-day dosing are ongoing. Kaletra capsules and solution are recommended to be stored in the refrigerator, but they are stable for up to 60 days at room temperature (77 F). However, avoid extreme heat and bright light.

Doctor

Kaletra, approved in 2000, is arguably the "gold standard" agent in the class. Kaletra, the only PI co-formulated with ritonavir, achieves remarkable drug levels which have resulted in excellent effectiveness and a very low rate of emergent resistance mutations. These features underlie the Federal recommendations of inclusion of Kaletra and two NRTIs among the (short) list of preferred regimens. Kaletra is associated with elevated cholesterol and triglyceride levels in approximately 30–35% of patients. These abnormalities of serum lipids can at times be severe and necessitate discontinuation of the agent. Like the majority of PIs, serum glucose levels may be elevated, particularly in those with a tendency towards diabetes. Kaletra has been used with numerous other PIs, particularly in the salvage setting.

—Stephen L. Becker, MD

Activist

Originally I thought this drug was a stupid idea—creating a drug that needs "boosting" to work. This concept however has given us a new way of using existing PIs—lowering pill burden and in some cases fewer side effects. Kaletra has demonstrated its ability to keep resistance at bay and to support PI-experienced patients who were unable to construct a viable regimen. Earlier this year, the Department of Health and Human Services (DHHS) guidelines named Kaletra as strongly recommended first line PI in the treatment of naïve patients. Those persons at risk for diabetes and heart disease particularly African Americans, Hispanics and obese individuals should be careful when using Kaletra and other protease inhibitors. You should have your glucose, cholesterol and triglycerides monitored closely. Recognizing that Kaletra does cause hyperlipidemia, Abbott is considering trials in which the patient is started on a statin agent at the initiating of antiretroviral therapy.

—Deneen Robinson

1x

Brand Name: Reyataz

Common Name: atazanavir sulfate

Class: HIV protease inhibitor (PI)
Standard dose: Two 200 mg capsules once daily, take with food. Treatment-experienced people should take 300 mg with 100 mg Norvir once daily. Available in 100 mg and 150 mg capsules. Take missed dose as soon as possible, but do not double up on your next dose.
Manufacturer contact: Bristol-Myers Squibb, www.reyataz.com, 1 (800) 272–4878
AIDS Treatment Information Service:
1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Limited data is available. However, most common include: dizziness and lightheadedness. Elevated levels of unconjugated bilirubin (produced by the liver) was reported in clinical trials in some individuals taking Reyataz. This may result in cases of jaundice (yellowing of the skin or eyes), reported in 3–6% of individuals taking Reyataz. However, no evidence of hepatoxicity (liver problems) was reported. These symptoms usually go away after you stop taking Reyataz.

All other protease inhibitors are associated with increased levels of cholesterol and triglycerides, except possibly unboosted Reyataz and these increased levels may be associated with heart disease. However, if Reyataz is boosted with Norvir these same changes in cholesterol and triglycerides may occur. Other possible side effects as seen in other PIs are 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 take with proton pump inhibitors (long-acting medicine for acid reflux): Prilosec-OC, Prevacid, Aciphex or Nexium. May be taken 12 hours apart from short-acting acid reflux medications (H2 inhibitors or blockers) like Zantac and Axid. Antacids like Mylanta must be taken at least two hours apart from Reyataz. Must be taken an hour apart from Videx, due to Videx's buffer. Boost with Norvir (300 mg Reyataz with 100 mg Norvir) when taking in combination with Sustiva. With Fortovase, use six Fortovase capsules with 400 mg Reyataz once-a-day with a high-fat meal. The levels of Reyataz are decreased by 40% when used at the same time as Viread. It remains uncertain how to overcome this interaction, though some leading clinicians have felt the the dose of atazanavir should be adjusted to 300 mg and boosted with 100 mg of ritonavir (Norvir), and still dosed once-a-day. This dose combination, recommended by the Reyataz manufacturer, is still in study.

Do not take with Tambocor, Rythmol, Versed, Halcion, Hismanol, Seldane, rifampin, ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form—serious interactions seen with dilation during gynecological exams), garlic supplements, and the herb St. John's wort. Reduce dose and frequency of rifabutin to 150 mg once-a-day. Do not use Zocor (simvastatin) or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastatin), Lescol, and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity.

Protease inhibitors increase blood levels of Viagra (sidenafil citrate), so initially the Viagra dose should be 12.5 mg (¼ of 50 mg tablet) and increased as needed and tolerated. It's recommended that people on PIs do not exceed 25 mg of Viagra in a 48-hour period because of potential for serious reaction.

Tips: Unconjugated bilirubin is not associated with either disease or liver toxicity, the usual cause of jaundice. Needs an acidic environment, so you can take it with orange juice or a cola (brush your teeth afterwards to get rid of the acid). Study is underway to see if a Videx dose adjustment is needed. Reyataz, approved in June 2003, is the second-newest protease inhibitor on the market. Reyataz is the only protease inhibitor shown to lead to the 150L mutation in HIV. This indicates a lack of cross-resistance to other protease inhibitors. The manufacturer does not recommend that it be taken with Crixivan because of the increased potential for jaundice.

Doctor

Atazanavir (ATV) is a newly approved once daily PI with, for some patients, distinct advantages over the other approved PIs. Unlike most agents in the class, ATV has thus far shown little adverse effects on serum cholesterol or triglycerides. It also has little potential to raise serum glucose. These are important benefits in a class with these characteristics and the potential for long term complications related to lipid and glucose abnormalities. ATV has good activity in treatment naïve and certain experienced patients. When used to treat patients with prior antiretroviral experience, ATV requires "boosting" with ritonavir. There are several drug interaction issues that require further evaluation. Co-administration of ATV with tenofovir significantly lowers ATV levels. Studies are under way to determine the most appropriate means of combining them. ATV requires food and gastric acidity for adequate absorption. The use of anti-acid agents, including those available over the counter, is contraindicated. Studies are ongoing to define ways that might overcome these interactions.—Stephen L. Becker, MD

Activist

Reyataz is the first protease inhibitor to offer once daily dosing for treatment naïve patients. Reyataz also boasts minimal impact on cholesterol or triglycerides unlike its fellow protease inhibitors.

—Deneen Robinson

Brand name: Lexiva

Common Name: fos-amprenavir sulfate

Class: HIV protease inhibitor (PI)
Standard dose: Two 700 mg tablets twice-a-day, no food restrictions. Treatment-experienced patients should use Lexiva twice daily with Norvir (700 mg plus Norvir 100 mg, twice-a-day). No food restrictions (may be taken with or without food) with either dosing. Take missed dose as soon as possible, but do not double up on your next dose.
Manufacturer contact: GlaxoSmithKline, www.lexiva.com, 1 (888) 825–5249
AIDS Treatment Information Service:
1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: The most common side effects include: nausea, rash, diarrhea, headache, vomiting, fatigue, mood disorders, abdominal pain, and mouth numbness. Rash occurred in about 19% of patients, but severe rashes were uncommon. If you experience a rash, notify your doctor. For mild or moderate rashes, your doctor may choose to continue Lexiva, with close follow-up and monitoring. Because Lexiva is a sulfonamide, it should be used with caution in patients with allergies to sulfa drugs. Side effects and laboratory abnormalities were similar when Lexiva was taken once or twice daily, with or without Norvir.

As seen with all other protease inhibitors are increased levels of cholesterol and triglycerides, except possibly unboosted Reyataz (atazanavir) and these increased levels may be associated with heart disease. Side effects and laboratory abnormalities were similar when Lexiva was taken once of twice daily, with or without Norvir. Other possible side effects are 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: Cannot be taken with Kaletra. Like all PIs, do not take with Tambocor (flecainide), Rythmol (propafenone), Versed, Halcion, Hismanol, Seldane, rifampin, ergot derivatives (such as Cafergot, Wigraine and Methergine, D.H.E. 45, in any form—serious interactions seen with dilation during gynecological exams), and the herbal supplement St. John's wort. Do not use Zocor (simvastatin) or Mevacor (lovastatin); lipid-lowering alternatives are Lipitor (atorvastatin), Lescol, and Pravachol (pravastatin), but they should be used with caution due to potential for liver toxicity. Oral solution contains alcohol, so do not use with Antabuse or Flagyl. Also avoid dihydropuridine calcium channel blockers.

Protease inhibitors increase blood levels of Viagra (sidenafil citrate), so initially the Viagra dose should be 12.5 mg (¼ of 50 mg tablet) and increased as needed and tolerated. It's recommended that people on PIs do not exceed 25 mg of Viagra in a 48-hour period because of potential for serious reaction.

Tips: Alternative dosing: Lexiva 1400 mg with Norvir 200 mg, both once daily. Studies have demonstrated that protease inhibitor-experienced patients should take Lexiva 700 mg with Norvir 100 mg, both twice daily. The once daily dosing is not recommended for treatment-experienced patients. It is important to take Lexiva exactly as your doctor instructs, and not to change dosing without discussing with your doctor. The FDA points out that the study comparing Lexiva/Norvir against Kaletra in protease inhibitor experienced patients was not large enough to show that the combination was clinically equivalent to Kaletra. Due to a drug interaction between Lexiva and Kaletra, these drugs can not be used together.

Lexiva is a "pro-drug" formulation of Agenerase. This means that when you take this pill, your body converts it to Agenerase. 700 mg of Lexiva is roughly equivalent to 600 mg of Agenerase. This new formulation is an improvement because it helps to make the pills smaller and easier to swallow. The new formulation also allows the drug to be given with fewer number of pills per day (4 per day). Approved in October 2003, Lexiva is the newest PI on the market. Pronounced "lux ee va."

Doctor

Amprenavir, and the newly approved pro-drug formulation, fos-amprenavir, have been studied in both treatment naïve and treatment experienced patients. Fos-amprenavir has substantial flexibility, and can be used as a sole PI, twice daily, or boosted with ritonavir and given either once or twice daily. When used in treatment experienced patients, fos-amprenavir should be dosed twice daily with ritonavir. In clinical studies, fos-amprenavir was found to be quite effective among patients with low CD4 count and/or high viral load. Fos-amprenavir has a favorable metabolic profile compared to several other PIs, but not to the same extent as atazanavir. Amprenavir has been used successfully when combined with Kaletra, despite a drug interaction. However the combination of fos-amprenavir and Kaletra have a significantly more profound interaction, making the use of this combination contraindicated. The eventual role for fos-amprenavir versus other PIs, particularly atazanavir, remains unclear and will likely be better defined by a series of upcoming clinical studies.—Stephen L. Becker, MD

Activist

Lexiva is the newest protease inhibitor on the market. It is actually the reformulation of the currently approved drug amprenavir. However, the new formulation greatly reduces pill burden and according to the manufacturer, GSK, this new formulation has fewer side effects and is easier to tolerate. It is important to note that GSK's clinical data demonstrates that this drug has shown good results in patients with advanced HIV disease and is more efficacious when boosted by Norvir (ritonavir). Nevertheless, the shadow of constant diarrhea and other GI side effects associated with amprenavir may be a difficult hurdle for this formulation to overcome. Hopefully this reformulation will have more success than the reformulation of saquinavir.
—Deneen Robinson

Photo not available due to experimental status

2x

Brand Name: Not yet established

Common Name: tipranavir

Class: experimental protease inhibitor
Standard dose: Dose not yet established because of experimental drug status, but studies are proceeding with a dose of two 250 mg capsules with two 100 mg capsules of Norvir, both twice daily. It will likely be dosed with food.
Manufacturer contact: Boehringer-Ingelheim, www.boehringer-ingelheim.com
AIDS Clinical Trials Information Service:
1 (800) TRIALS–A (874–2572)

Potential side effects and toxicity: Mostly gastrointestinal-related: mild diarrhea, nausea, vomiting and fatigue. In clinical trials symptoms have been managed by having a light snack with the drug. Other side effects include headaches, dry mouth and dizziness. This dose of tipranavir was fairly well tolerated in Phase II studies, with few patients needing to discontinue this combination due to side effects, but full side effect profile isn't usually determined until drugs move into Phase III. See ritonavir for more details on potential side effects.

Potential drug interactions: Not yet finalized. This drug is metabolized by the liver (same as most of the other protease inhibitors). It is only dosed with ritonavir. No dose adjustments are likely to be necessary when given with didanosine, tenofovir or efavirenz. See ritonavir for the drug interactions possible. Studies for use with other protease inhibitors are underway.

Tips: Tipranavir is the first non-peptidic protease inhibitor (NPPI) in development for the treatment of HIV infection (a different chemical structure). Initial studies indicate that tipranavir may be active against strains of HIV that are already resistant to currently available peptidic protease inhibitors. As resistance becomes more and more an issue for treatment experienced individuals, this type of drug may offer hope. Phase III studies are being conducted in patients with documented drug resistance to HIV, using an optimized background regimen. Find a clinical trial site with the drug!

Doctor

Tipranavir is an investigational protease inhibitor being studied exclusively in treatment-experienced patients. This agent will have to be combined with ritonavir to have manageable pill burden (currently two tipranavir capsules with two ritonavir capsules twice daily). The cholesterol and triglyceride changes with this combination appear similar to low-dose ritonavir alone, but this is early data. The main side effect with this one may end up being stomach related (diarrhea and abdominal pain), but this is not yet finalized. Studies are ongoing and some sites have tipranavir available through an expanded access protocol.

—Patrick G. Clay, PharmD

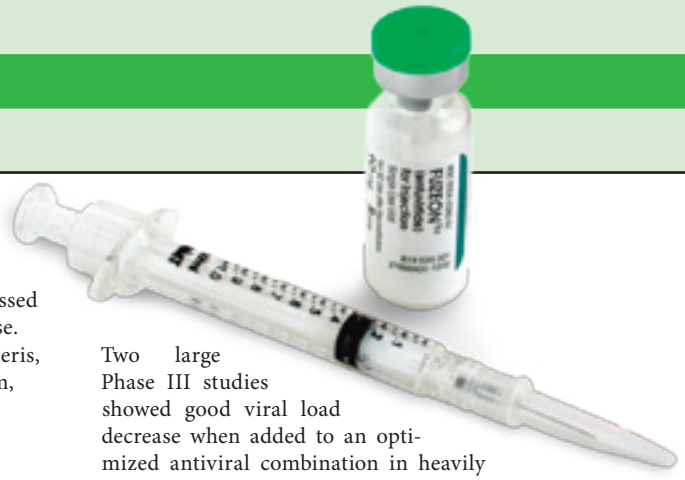
Activist

Statement not provided.

2x

Brand Name: Fuzeon

Common Name: T-20, enfuvirtide



Class: fusion inhibitor
Standard dose: One subcutaneous injection of 90 mg (1 ml) twice daily into the upper arm, thigh or abdomen. No food restrictions (take with or without food). Take missed dose as soon as possible, but do not double up on next dose.
Manufacturer contact: Roche Pharmaceuticals and Trimeris, www.rocheusa.com, www.trimeris.com, www.fuzeon.com, 1 (877) 4–FUZEON (438–9366)
AIDS Treatment Information Service: 1 (800) HIV–0440 (448–0440)

Potential side effects and toxicity: Most common include: Injection Site Reactions (ISRs) occur in virtually all patients. The severity of reactions is variable, and for most is mild to moderate. Symptoms could include itching, swelling, redness, pain or tenderness, hardened skin or bumps; others include headache and fever. Allergic reactions are possible. In studies, pneumonia happened more often in the patients on Fuzeon. It is unclear if this was related to the use of Fuzeon. Report cough, fever or trouble breathing to your healthcare provider right away.

Potential drug interactions: To date none that require dose adjustment have been reported.

Tips: To minimize injection site reactions, inject slowly and apply a gentle massage after injection. 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). Never shake—it will foam. Follow instructions to avoid infection. ISR may worsen when injection is repeated in the same spot or given deeper than intended for example, into the muscle. Fuzeon can be taken at the same time as other anti-HIV drugs. Rotate injection sites. Never inject into moles, scars, bruises or the navel.

Fuzeon 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 likely 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 in addition to Fuzeon and both genotype and phenotype tests.

Trimeris also has another fusion inhibitor in development, T-1249 in Phase II, that may work when/if resistance to Fuzeon develops. It is hoped that T-1249 will be given as an injection 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. In Phase I/II clinical trial of T-1249, no treatment-related, clinically important laboratory abnormalities occurred and no dose-limiting toxicities were identified. Three serious adverse events possibly related to T-1249 occurred: Grade 4 neutropenia (25 mg once-a-day, or QD), hypersensitivity reaction (25 mg twice-a-day, or BID), and fever associated with injection site reaction (150 mg QD).

Doctor

Enfuviritide (T-20) is the only available agent in this promising and novel class of drugs. Used only in the experienced patient population, T-20 when combined with at least one other active agent has significant and durable benefits. Administration by twice daily subcutaneous injection and its high cost have limited the use of this agent. The challenge posed by T-20 and its development program is how to usefully preserve other active antiretroviral agents for use in a T-20 based regimen. As other agents, including oral agents, in this class are developed, it can be hoped that clinicians will have a strategic approach to HIV treatment that allows drugs such as T-20 to be paired with other effective agents.

—Stephen L. Becker, MD

Activist

This injectable came along at a most opportune time to save the lives of those with little or no treatment options. It also came with unique issues. It is very costly—$20,000–25,000 per year. Roche says this cost is necessary because of the complications of manufacturing. Also, the physician must demonstrate that the patient is resistant to at least two classes of medications and has used medications from all three classes. Because of the state of treatment for those initially using T-20, the rigorous dosing schedule of injecting medication twice daily has been met with few reservations. Beware of the injection site reactions. Follow the company's suggestions to limit or prevent these reactions. Also, many say that using a vibrator on the injection site can limit the knots that sometimes form. The company hopes that the future of T-20 will include patients who are newly infected with HIV. Because of the high resistance of so many of the patients currently taking Fuzeon, combination therapy mirrors monotherapy in that the patient only has one drug they are not resistant to.—Deneen Robinson

A GUIDE FOR UNDERSTANDING THE GUIDELINES

by Matt Sharp

This issue of *Positively Aware* is proof that there is much to know and understand about the 22 current anti-HIV drugs, including side effects, the complexity of drug resistance and overall treatment standards. As the years go by and HIV treatment incrementally yet substantively changes, the need for guidelines to assist physicians and people living with HIV is needed. The complexity of HIV disease and the scope of the pandemic have required recommendations from a panel of HIV experts to help guide those less experienced, or for those who just may need reference.

The Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents are developed by the Panel on Clinical Practices for Treatment of HIV Infection and convened by the Department of Health and Human Services (DHHS). The panel consists of physicians, researchers, clinicians and advocates for people living with HIV as well as participants from the DHHS. First published in 1998, the guidelines have been revised nine times since then, the newest version released in November 2003. Prior to these guidelines, HIV treatment decisions were based on miscellaneous information that had to be gathered from medical journals and physician experience.

Guidelines exist for many diseases from obesity to heart disease. The need for a guide is crucial for management and treatment. HIV is no exception, especially given the relative newness of the disease and ever changing treatment options. The Antiretroviral Guidelines are not rules, since treating HIV-positive people successfully depends on many individual factors. They are

meant to be a resource for information and an "understanding" of HIV disease according to the recent data—but are not a mandate on how to treat. The Guidelines always highlight the revised text which reflect changes in the growing knowledge base in HIV and AIDS. Revisions include the latest information based on careful review of clinical trial information.

The detailed text is useful for physicians, treatment advocates and people with HIV alike. Most of the Guidelines are charts that break down what the text says in the beginning of the document. It is broken up in sections that include: CD4 and viral load testing, resistance testing, considerations on when to start therapy, adherence, considerations in those who have never taken HIV therapy ("naïve"), drug related adverse events, interruption of therapy, considerations for changing therapy (and the available options) treatment in acute HIV infection, adolescents, pregnant women and concerns about HIV transmission.

CD4 T-cells and viral loads

CD4 T-cells and viral load testing are diagnostic tests that tell us how the virus is progressing and how intact our immune systems are, which in turn inform us about treatment decisions. Tests should be repeated to confirm results because one single result may not always tell the full story. Thinking of the results as a "trend" over time is more meaningful than one single result. T-cells should be tested at the first diagnosis of HIV and every 3 to 6 months thereafter.

Since there are three viral load tests approved by the FDA (Food and Drug Administration), providers should use the same type of test each time with patients upon starting or changing anti-HIV medications. The test should be repeated 2 to 8 weeks after starting therapy to see if the numbers have gone down, then again every 3 or 4 months to show that the medications are still working. The guidelines also advise how much an increase or decrease in virus load is substantial enough to justify a treatment decision.

Resistance testing

The resistance section of the guidelines is entirely new because understanding HIV resistance is a relatively new science. Although complicated, resistance testing should give a good indication of which drugs to use when combined with the individual's complete medical history. The tests are used for those who need to start treatment and those who need to change because their anti-HIV medicines are no longer working. Two types of resistance tests are best used in conjunction to give the best result. The *genotype* analyzes what specific mutations are present in HIV with sophisticated high technological equipment. The *phenotype* looks to see what concentrations of antiretroviral drugs are needed to control HIV. Both can help make treatment decisions, but only if you have detectable virus to analyze, at least 1,000 copies viral load.

Limitations of the tests are that they are expensive, lack uniform quality assurance, and can be difficult to interpret, although results are nicely explained on computer print-outs. If mutated viral populations of less than 20% exist in the entire pool of HIV in the body, resistance probably won't be detected. One thing to remember is that you should be taking all of your anti-HIV medicines at the time of your resistance test to get the most accurate result.

Starting therapy

The time to start anti-HIV drugs seem relatively clear in the Guidelines, however beginning treatment is never an easy decision. According to the Guidelines, people with less than 200 CD4 cells who are experiencing symptoms should begin therapy. Those with less than 350 CD4 cells or a viral load over 55,000 should be "offered" treatment. Those people over 350 CD4 cells or under 55,000 virus copies can afford to wait; however, some experts in the Guidelines would recommend treatment. Despite these particular cutoffs, any person with HIV who has had to start AIDS drugs knows that he or she must simply be ready and willing.

The goals of HIV therapy can help inform decisions to start therapy. Antiretrovirals must be able reduce viral load to as low as possible for as long as possible. They must also restore or preserve the immune system, improve quality of life, and reduce sickness and death. Anyone who has been treated with anti-HIV medicines knows there is a conundrum with these goals as sometimes the medicines can cause toxicities. But the tradeoff with untreated virus is usually progression of HIV, further illness, and death.

It is often said that your first regimen is your most important one; however, which drugs to take in your first regimen is not always easy to decide. Factors to remember are potency and durability, related toxicities and possible drug interactions, and how often does the drug need to be taken and how many pills are required. Looking at these factors one can see it is important to remember the individual in planning the first regimen. The Guidelines categorize antiretrovirals as "preferred" and "alternative." There are several preferred regimens and many more alternative ones. There are also certain regimens listed as "not recommended" because some drugs can be toxic when used together. Up-to-date information on once-daily therapies, drugs not recommended for a first regimen, drug-drug interactions, and initiating treatment in pregnant women or women who may become pregnant is included in the Guidelines. Other important information is written in fine print, such as the fact that Zerit has been associated with facial wasting.

Treatment interruptions

Interrupting HIV treatment usually happens due to toxic side effects, drug interactions, or (obviously) if medication runs out. Also, women who become pregnant may consider interrupting therapy for the first three months of pregnancy. The Guidelines do not recommend interrupting therapy due to failure. Anytime HIV drugs are stopped, they should be stopped altogether and then started together again because of resistance.

When treatments don't work or if you cannot tolerate them anymore due to abnormal lab values, intolerable side effects, or drug interactions, a change might be necessary. The Guidelines recommend changing therapies if you see an increase in viral load from undetectable to detectable, a failure to increase CD4 cells by 25-50 in the first year of treatment, or if any new AIDS related illness occurs. What drugs to change to can be the most complex decision a patient and their doctor will make together. Ideally, three drugs that a person's virus is still sensitive to should be used in the new regimen. Often, in treatment experienced patients, three or even two new drugs are simply not an option. In that case it may not make sense to change therapies if the viral load is stable. Consider, however, experimental therapies in clinical trials.

The Guidelines have an extensive section on management of treatment experienced individuals that includes the definition of treatment failure, and how to manage patients depending on why the drugs stopped working. There are also sections explaining the current information on HAART (Highly Active Anti-retroviral Therapy) associated clinical events such as liver disease and lactic acidosis, a treatment related side effect that can be fatal. Other adverse events discussed are diabetes, fat maldistribution, and hyperlipedemia, conditions known today as lipodystrophy. There are even sections on acute HIV infection, treatment in adolescents and pregnant women.

Not written in stone

The Guidelines are an ever-changing document that reflect the current standards in HIV treatment and are an important guide to assisting physicians in making responsible treatment decisions. To read the full document go to the DHHS website: http://AIDSinfo.nih.gov. It has information on all the AIDS guidelines available, including adults and adolescents, pediatric, perinatal, post exposure prophylaxis, HIV complications and HIV testing. Supplements are also available for women and for pregnancy. You can download them or order them to be sent for your own personal use.

Matt Sharp is the Director of Treatment Education at Test Positive Aware Network.

Recommended Antiretroviral Regimens for Treatment of HIV in Antiretroviral Naïve Individuals as established by the *Guidelines for the Use of Antiretroviral Agents in HIV-1 infected Adults and Adolescents*, November 2003, http://aidsinfo.nih.gov

NNRTI-Based Regimens	
Preferred Regimens	Sustiva + Epivir + (Retrovir or Viread or Zerit*) —except for pregnant women or women with pregnancy potential**
	Sustiva + Emtriva + (Retrovir or Viread or Zerit*) —except for pregnant women or women with pregnancy potential**
Alternative Regimens	Sustiva + (Epivir or Emtriva) + Videx —except for pregnant women or women with pregnancy potential**
	Viramune + (Epivir or Emtriva) + (Retrovir or Zerit* or Videx)
PI-Based Regimens	
Preferred Regimens	Kaletra + Epivir + (Retrovir or Zerit*)
Alternative Regimens	Amprenavir/Norvir# + (Epivir or Emtriva) + (Retrovir or Zerit*)
	Atazanavir + (Epivir or Emtriva) + (Retrovir or Zerit*)
	Crixivan + (Epivir or Emtriva) + (Retrovir or Zerit*)
	Crixivan/Norvir# + (Epivir or Emtriva) + (Retrovir or Zerit*)
	Kaletra + Emtriva + (Retrovir or Zerit*)
	Viracept + (Epivir or Emtriva) + (Retrovir or Zerit*)
	Saquinavir (hard-gel or soft-gel)/Norvir + (Epivir or Emtriva) + (Retrovir or Zerit*)
Triple NRTI Regimen – Only when an NNRTI- or a PI-based regimen cannot or should not be used as first line therapy	
Only as alternative to NNRTI- or a PI-based regimen	Ziagen + Epivir + Retrovir (or Zerit*)

*Higher incidence of lipoatrophy, hyperlipidemia, and mitochondrial toxicities reported with Zerit than with other NRTIs
**Women with child bearing potential implies women who want to conceive or those who are not using effective contraception
#Low-dose (100-400 mg) Norvir

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compiled by Jeff Berry

**indicates brief news item*

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Taking Giant Steps Forward in Antiviral Drug Treatment

by Daniel S. Berger, MD

The development of drugs used to treat people with HIV have historically been based on safety, as well as their effect on reducing viral load. Twenty antiviral agents are currently approved in the U.S. (not counting combination pills) and the ability to choose from multiple agents within three of the main classes of antivirals has stirred up the competition among drug companies to win more market share.

For many newly infected patients or the antiretroviral naive, treatments have become more simplified with fewer pills while improving potency. However, for the heavily treatment-experienced individuals, the challenge of maintaining virologic effect while reducing toxicities is indeed an ongoing task.

More patients need agents to combat the many problems that are often experienced with long-term treatment. Pharmaceutical companies are well aware of these difficulties that run the gamut from high pill burdens, body shape abnormalities, elevated cholesterol and triglycerides to the high degree of resistance to currently available therapies. Thus a war against the evils of long-term therapy is being fought by the pharmaceutical industry with drug development, because companies know that newer agents that successfully improve patient tolerability, safety, potency and effect will become more prescribed. This ultimately leads to greater profitability among their pharmaceutical sales. This article will review the new "niches" that can be ascribed to by various newer agents and the advantages available over older counterparts and previous drug combination regimens.

New Strategies of Attack: Entry and Integrase Inhibitors

One solution to keep HIV suppressed (lower viral load) after failing multiple treatment regimens includes developing new sites from which to strike at the virus. People whose virus has become resistant to current treatment, and those who face this predicament, are growing daily. Individuals who have resistance to present drugs often are cross-resistant to other agents within those same classes, but are unlikely to be resistant to an entirely new class of treatment. The targets of HIV integrase and of HIV's entry into cells have become the latest tactics for developing newer therapies.

A war against the evils of long-term therapy is being fought by the pharmaceutical industry with drug development.

The classic drug classes—nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors and protease inhibitors—all reduce HIV replication from within the human cells (CD4+ T-cells) during its life cycle. However, new drugs are being developed to stop HIV before it gains entrance to human cells; each drug works on one of the three specific steps that are required for the virus to enter the cell.

1. HIV attachment to the CD4 receptor
2. Chemokine receptor attachment using either the CCR5 or CXCR4 chemokines
   (steps 1 and 2 are required for HIV attachment to the CD4+ T-cell prior to fusion)
3. Fusion of the virus and cell membranes

The first drug that attacks HIV before entry into the CD4+ T-cell was developed and approved this past year. T-20 or enfuvirtide (Fuzeon) is a multiple amino acid chain (polypeptide) that blocks fusion of HIV onto the CD4+ T-cells. Because of Fuzeon's chemical structure, digestive acids can break it down, thus not allowing for oral administration. It is self-administered by subcutaneous injection twice daily. The patients who participated in the pivotal clinical trials were those with high levels of resistance to all available classes of antiretroviral drugs (studies TORO 1 & 2). These studies demonstrated significant viral load suppression and improvements in CD4 T-cells that was durable for at least 48 weeks. Studies looking at both T-20 injections to be injected only one time per day are soon to be underway. A second candidate polypeptide drug, T-1249, is being developed for individuals who may have resistance to T-20 and as a more potent first-line fusion inhibitor. Hopefully, T-1249 will be administered as once daily injections. Phase II trials are soon to begin.

PRO 542 is a CD4 receptor attachment inhibitor that is administered by injection because the chemical structure is similar to immunoglobulins. It has a particularly

long half-life (time to metabolize half the drug), and dosing may be perhaps only once or twice weekly. Only preliminary studies have been conducted thus far.

SCH-D is being developed as the first oral entry inhibitor that is a chemokine receptor (CCR5) antagonist. A small pilot study with a previous compound, SCH-C, had demonstrated a cardiac conduction abnormality in one patient. Schering-Plough eventually decided on pursuing Phase II with its other candidate SCH-D. Long awaited Phase II clinical trials are being planned for the spring of 2004. Studies demonstrated potent dose dependent anti-viral effects for these agents.

Another target for attack focuses on the HIV integrase enzyme required for the assembly and processing of its viral DNA strands. Integration is an additional component of the HIV replication life cycle. Integrase inhibition has eluded scientists for many years, but finally several compounds are nearing human testing. Integrase inhibitors demonstrate antiviral activity in preliminary studies of monkeys infected with SIV (simian immune deficiency virus), showing extraordinary potency and effect with various integrase compounds.

Less Pills and Reduced Dosing

Lowering the number of pills and dosing has proven to help maintain a patient's ability to continue taking their medications long-term.

Tenofovir (Viread) was the first drug developed as a one pill a day treatment. Since that time, various companies are attempting to compete by reformulating and condensing the number of pills and or doses. Videx has been reformulated to Videx-EC; 3TC + abacavir (Epivir + Ziagen) is being formulated to combine both agents and doses into one pill taken once per day (the "Easy Tablet"). FTC (Emtriva) is another agent administered as one pill, once-a-day; it is also being co-formulated as a one-pill combination of FTC/tenofovir (Emtriva/Viread) taken once per day.

Boosting blood levels of protease inhibitors with ritonavir builds a pharmacokinetic wall to oppose viral resistance and has become a dramatic advance in treatment.

Of the non-nucleoside RT inhibitors (NNRTIs), efavirenz (Sustiva) originally had come to market as three capsules once daily and was reformulated into one pill. Also, many clinicians are dosing nevirapine (Viramune, usually one pill twice daily) to be taken as both pills once per day.

Several protease inhibitors have also jumped on the once-daily bandwagon due to pharmacokinetics that support their once-daily dosing.

Atazanavir (Reyataz)is the first once-a-day protease inhibitor. It was approved in late June of 2003 and is administered as two 200 mg capsules once a day or alternatively with ritonavir boosting—(two 150 mg capsules atazanavir combined with 100 mg of ritonavir). Additionally, boosting may be required when using atazanavir combined with tenofovir and certain NNRTIs, because of the pharmacokinetic changes. Uncharacteristic for protease inhibitors, atazanavir has not been shown to increase serum lipids (blood fat) such as cholesterol, LDL cholesterol or triglycerides. This may have very important advantages long-term for patients on atazanavir in reducing their coronary risk as compared to patients taking other protease inhibitors.

Fos-amprenavir (Lexiva) has just been approved in late October 2003. It is a phosphate-ester prodrug of amprenavir (Agenerase). As a ritonavir-boosted protease inhibitor, fos-amprenavir can also be dosed once daily as well as twice daily. Additionally, it appears to be well tolerated.

Resistance and More Resistance

Drug development and the construction of better regimens for those individuals who have resistance to antiretroviral agents, testing and treatment have evolved into a high level of sophistication. Assays for the testing and detection of viral RNA have become more sensitive with most clinicians using the below 50 copy number as standard. Genotyping and phenotyping of a patient's HIV resistance pattern and their susceptibility to different agents have become the norm when making treatment decisions. Boosting blood levels of protease inhibitors with ritonavir builds a pharmacokinetic wall to oppose viral resistance and has become a dramatic advance in treatment. Moreover, double-boosted protease inhibitor use has become more commonly used with the more highly experienced patients in our practice. And finally, treatment interruptions to facilitate the materialization of wild type virus and to suppress quasi-species that have resistance mutations have also been used on occasion.

Protease Inhibitor Boosting

In part to head off the problem of resistance, various boosted protease inhibitor

combinations have been formally studied in controlled clinical trials and have shown favorable options for patient therapy. Some brief examples of studies are listed here (*see Table 1*).

MaxCmin 1 is a study using patient groups with various levels of antiretroviral experience. The intent-to-treat analysis of ritonavir-boosted saquinavir showed more significant viral load suppression over boosted indinavir. The MaxCmin 2 study, however, comparing boosted saquinavir against boosted lopinavir (Kaletra), showed a greater percentage of patients on the Kaletra arm to have viral loads below 400 copies. However, the on-treatment analysis for achievement of viral loads less than 50 copies favored boosted saquinavir. Neither values were found to be statistically significant, however.

Of the trials with the newer protease inhibitors, the Context study randomized patients who had already taken one or two prior protease inhibitors to once-daily boosted fos-amprenavir (Lexiva) versus twice-daily boosted fos-amprenavir versus boosted lopinavir (Kaletra). The data of the 24-week results and outcome was affected by a difference in treatment experience between the three arms. Although the lopinavir arm was associated with better viral load suppression, this arm had less nucleoside and less protease inhibitor experienced patients.

Finally, the BMS 045 trial studied boosted atazanavir (Reyataz) versus boosted lopinavir (Kaletra) versus the combination of saquinavir and atazanavir in patients who had exposure to all three classes, and who failed at least two prior regimens. The results favored both ritonavir-boosted regimens over the saquinavir/atazanavir combination.

These are all examples of studies demonstrating practical applications of boosting protease inhibitors to achieve more maximal suppression and build a greater barrier for resistance development.

Table 1

Studies Comparing Ritonavir-Boosted Protease Inhibitor Combinations: Opportunities for their Practical Use in HAART Regimens

Boosted Protease Inhibitors	Study
Ritonavir-boosted saquinavir vs. Ritonavir-boosted indinavir	MaxCmin 1
Ritonavir-boosted saquinavir vs. Ritonavir-boosted lopinavir (Kaletra)	MaxCmin 2
Ritonavir-boosted fos-amprenavir QD vs. Ritonavir-boosted fos-amprenavir BID vs. Ritonavir-boosted lopinavir (Kaletra)	Context
Ritonavir-boosted atazanavir vs. Ritonavir-boosted lopinavir (Kaletra) vs. atazanavir + saquinavir	BMS 045

New agents at the forefront

Also heading off resistance are new drugs in developement that have novel mutations. Tipranavir is one of several protease inhibitors being studied in pivotal clinical trials expecting to gain eventual FDA approval. As a nonpeptidic compound, it is the farthest along in clinical trials. Tipranavir has been shown to be active against resistant HIV strains. It is dosed as a boosted protease inhibitor and is administered twice daily. Tipranavir is currently in Phase III testing. Anecdotally, patients who are participating in a clinical trial with tipranavir treatment at Northstar in Chicago are demonstrating good virologic effect.

Tibotec-Virco, a Belgian company, has developed several compounds that demonstrate potent antiviral activity. Their candidate protease inhibitor, TMC-114, has only recently started undergoing the first trials in the U.S. (Phase II) and has shown remarkable antiviral activity against almost any level of resistant mutations in laboratory testing.

Tibotech's non-nuke, TMC-125, is being planned for Phase II study in March of 2004. An additional non-nucleoside reverse transcriptase inhibitor, capravirine, developed by Agouron Pharmaceuticals, is in Phase III trials.

Body Fat and Lipodystrophy

While HIV-positive persons are being administered life-long treatment, the potential for more long-term problems and side effects has grown. Prior to HAART (highly active antiretroviral therapy), wasting syndrome was the prevailing nutrition-related evil among those with AIDS. However, since newer, more effective therapies have resulted in improved long-term survival, patients must now contend with body shape

abnormalities and redistribution of fat that are associated with metabolic problems. The physical abnormalities have impacted individuals psychologically, but it is probable that the elevated lipids (blood fat) will increase cardiovascular disease risk.

The various antiviral drugs are ranked in clinicians' minds by their potential to cause metabolic and lipodystrophic problems. As long-term use of certain nucleosides have been shown to pose higher risk for developing facial atrophy, their usage has dropped dramatically. Experienced physicians cognizant of the many lipodystrophy studies have synthesized for themselves information from many studies comparing metabolic and body habitus changes with certain treatment regimens. This has eventually translated into applying the results in the clinics with their patients. As with other side effect profiles, various agents are selected based on toxicities of other drugs.

Examples of important clinical trials include study GS-903, which compared tenofovir and d4T in a Sustiva-based regimen. The results of GS-903 showed an increased incidence of elevated lipids and lipodystrophy related problems in the d4T arm. In study BMS-043, atazanavir treatment demonstrated a decline in cholesterol and triglycerides. The potential implications are obvious: atazanavir may eventually be shown to be associated with less lipodystrophy problems, but further study is needed. Drug development needs to include investigating the potential occurrence of lipodystrophy-related complications for the many newer agents in clinical trials.

Conclusion

Treatments have altered the course of persons infected with HIV so that individuals on optimal treatment no longer need to confront mortality on a daily basis. However, long-standing HIV infection and their medications have posed many challenges for physicians and their patients. Drug development and treatment has progressed dramatically to the point where newly infected individuals can start treatment that is low in complexity yet more potent. Highly experienced patients can be hopeful because they have new sophisticated options with further upcoming choices that are approaching in the near future.

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

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TPAN Events Calendar

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

January 2004

Date	Time	Event
Wednesday 7th	7:30–9:00 pm	Committed to Living Series – Resistance Testing. Understand the finer points to drug resistance and mutations. Sponsored by Agouron Pharmaceuticals.
Monday 19th		Office closed in observance of Martin Luther King, Jr. holiday.
Tuesday 27th	6:30–8:00 pm	The new generation of protease inhibitors. Daniel S. Berger, MD, of NorthStar Healthcare will discuss new treatment options with this drug class. Sponsored by GlaxoSmithKline.
Thursday 29th	6–10 pm	PULSE – the monthly party for the HIV community at Berlin Nightclub. This month will feature guest bartender Charles Clifton, executive director of TPAN.

February 2004

Date	Time	Event
Thursday 4th	7:30–9:00 pm	Committed to Living Series – Exercise and HIV. Understand the importance of exercise in the management of HIV disease. The forum will include demonstrations on important exercises, so dress comfortably. Sponsored by Abbott Laboratories.
Thurs. - Sat. 12th–14th		Fireball! – the annual event benefiting Chicago area GLBT and AIDS service organizations. Please visit www.heartsfoundation.org for information on the Fireball Festival.
Thursday 26th	6–10 pm	PULSE Party at Berlin Nightclub
Saturday 28th		Will Clark's Bad Boys Burlesque - Chicago – Gentry's on State. An afternoon of decadent entertainment benefiting TPAN.

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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

Medical Clinic

HIV/STD screenings and full medical care for HIV positive clients is available. Program is offered by Access Community Health Network. Call for an appointment. 10:30 am–6 pm.

TPAN Daytimers

A support group for people with HIV who prefer to meet during the day. 10:30 am–12:30 pm.

HEALTH (HIV Empowerment And Living Together with Hepatitis)

New support group for people living with HIV and hepatitis. HEALTH focuses on therapy and treatment concerns of people who have experienced HBV/HCV/HIV co-infection. Meets Monday 1/12, 1/26, 2/9, and 2/23 from 7:30–9 pm.

Spirit Alive!

Through a collaborative effort of AIDS Pastoral Care Network (APCN) and TPAN, Spirit Alive! fosters discussions on topics such as hope vs. despair or strength in times of adversity. Meets from 7:30–9 pm.

Tuesday

Yoga

All levels of yoga are welcome. Meets from 10–11 am.

Positive Progress

A peer-led group for HIV positive individuals in recovery. Special emphasis is placed on sobriety as a priority to effectively living and dealing with HIV. Meets from 7–9 pm.

Living Positive

HIV positive gay men discuss how being positive affects life and relationships. Socials and speakers on occasion. Meets from 7:30–9 pm.

Wednesday

Medical Clinic

See description on Monday. Call for an appointment. From 10:30 am–6 pm.

Wednesday continued

Needle Exchange Program

Through a collaborative effort of Chicago Recovery Alliance and TPAN, a free, anonymous, legal syringe exchange and HIV/AIDS prevention is offered Wednesdays from 5–7 pm, or by appointment.

SHE (Strong, Healthy and Empowered)

HIV positive women discuss needs, concerns and issues facing women with HIV. Meets Wednesdays from 7:30–9 pm.

Poz Leathermen

New support and social group for HIV positive leathermen and friends. Meets from 7–9 pm.

Yoga

All levels of yoga are welcome. Meets from 7:30–8:30 pm.

Thursday

TPAN Daytimers

See description on Monday. Meets from 10:30 am–12:30 pm.

Needle Exchange Program

See description on Wednesday. Thursdays from 2–5 pm, or by appointment.

BUS (Brothers United in Support)

Support group for HIV positive gay and bisexual men of African descent. Monthly socials and speakers on occasion. Meets from 7–9 pm.

Positive Now

Support group for all HIV positive individuals who seek support, education and the opportunity to share their experiences in a relaxing, empowering environment. Special emphasis is placed on newly diagnosed transitioning. Meets from 7–9 pm.

Pulse at Berlin

A weekly social for HIV positive individuals and friends. 6–10 pm at Berlin, 954 W. Belmont, Chicago.

Friday

Needle Exchange Program

See description on Wednesday. Fridays from 2–5 pm, or by appointment.

Safe Passage

A support group for young adults (ages 18–24) who are HIV positive. Meets from 7–9 pm.

Scheduled By Appointment

FASN (Family AIDS Support Network)

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

Individual Counseling

Licensed professional provides individuals with one-on-one counseling on Mondays. Call APCN at (773) 394-7063.

Peer Support Network/Buddy Program

Trained volunteers provide one-on-one peer, emotional support to individuals living with HIV. Call Jim at (773) 989-9400.

Speakers Bureau

Individuals are available to community groups to educate peers on HIV, safer sex, and harm reduction. Call Matt at (773) 989-9400.

TEAM (Treatment, Education, Advocacy and Management)

This peer-led program integrates secondary prevention and treatment education to provide individuals the training and knowledge to more successfully support other individuals impacted by HIV. Call Montré at (773) 989-9400.

Reiki

Energetic healing practice that utilizes hands-on touch and focused visualization. Meets Tuesdays and Thursdays by appointment only from 2–5 pm.

Miscellaneous

livingpos18to24@aol.com

An AOL chat room for young adults (ages 18–24) who are HIV positive. Monday through Friday from 3–5 pm.

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The Journal of Test Positive Aware Network

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- Public health clinics.
- Public or private mental health facilities that treat the HIV community.
- Gay and lesbian community organizations.

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