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treatment

MISSION

The Center for AIDS Information & Advocacy empowers people living with HIV to make informed decisions about their health care by providing the latest research and treatment information and by advocating for accessible, affordable, and effective treatment options until there's a cure.

About *HIV Treatment ALERTS!*

HIV Treatment ALERTS! is a publication of The Center for AIDS Information & Advocacy (The CFA). This newsletter is intended for those affected by HIV and their caregivers. The statements and opinions expressed in this newsletter do not imply recommendations or endorsement. Always consult your doctor before altering a prescribed drug regimen or taking any drug or supplement.

HIV Treatment ALERTS! is published twice a year. The print version of the newsletter is available for free at The CFA's L. Joel Martinez Information Center, various AIDS service organizations, some physician offices and health clinics, or by mail. Access to the newsletter is available online from The CFA website (***www.centerforaids.org***).

The CFA also publishes Research Initiative/*Treatment Action!* (RI*TA!*). RI*TA!* is a literature-review journal that covers issues in HIV research and policy. This and other publications are available on The CFA website or can be requested by mail (see contact information below). CFA publications are supported in part with unrestricted funding from AIM Investments, CFP Foundation, Gilead Sciences, and GlaxoSmithKline.

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Highlights

Chicago, September 17-20, 2007

47th Interscience Conference
on Antimicrobial Agents and Chemotherapy

Every year, the ICAAC follows on the heels of the Annual Conference on Retroviruses and Opportunistic Infections (CROI; *HIV Treatment Alerts!*, June 2007), even though the ICAAC is a much larger meeting than the Retrovirus Conference. The ICAAC draws more than 12,000 medical professionals from around the globe. It also appeals to a much broader medical community of physicians, researchers, and other health-care providers who are interested in the problem of infectious diseases, including, but not limited to, HIV and AIDS. The news throughout this year has focused on several key areas, and our coverage in this issue of *HIV Treatment Alerts!* will follow up on the most recent news relating to:

- Drugs in development - newly approved and coming soon
- Drug treatment interruptions - long-term effects
- Treatment side effects - control of **opportunistic infections** and conditions not related to AIDS

Update on New Drugs

Chemokine Antagonists

Researchers presented information from several studies of a new class of drugs known as **chemokine antagonists**. By blocking something called the CCR5 receptor, a cell protein that HIV uses to infect T-cells, this kind of drug hinders HIV from attaching to the surface of T-cells. This action prevents the virus from infecting healthy cells. The newly approved chemokine antagonist, ***maraviroc*** (*HIV Treatment Alerts!*, June 2007), now known as Selzentry™, was one of the main topics discussed at the ICAAC. Following up on the 24-week data presented to the United States Food and Drug Administration (FDA) when the agency recently approved the

drug, Jay Lalezari, from the University of California San Francisco, highlighted findings from the MOTIVATE 1 study (Abstract H-718a) after 48 weeks of data collection. The 585 patients in the Phase 3 study of maraviroc were **randomized** to receive placebo, or 300 mg maraviroc once daily, or 150 mg maraviroc twice daily. Everyone in the study received an **optimized background therapy** combination that was selected according to which drugs they were **resistant** to. Almost half of the patients who had viral loads below 50 copies at 24 weeks were able to maintain this level over a longer period of time. The great news is that the twice-daily dose was very well tolerated with very little evidence of **toxicity**. This is especially encouraging because the investigation of another chemokine antagonist, ***alpaviroc***, was discontinued after it was discovered that the drug caused severe liver problems. Only 2 individuals out of the thousands of people treated with maraviroc have had the same problem.

PRO 140, a new chemokine antagonist in very early development, showed promising results (Abstract H-716). Progenics Pharmaceuticals, the manufacturer of the drug, conducted a clinical trial at 10 sites in the United States, evaluating 3 single **intravenous** doses of PRO 140: 0.5 mg/kg, 2.0 mg/kg, or 5.0 mg/kg of body weight to **placebo**. A total of 39 HIV-positive patients, none of whom had used HIV medications in the past, were enrolled in the trial. The purpose was to see if the drug reduced viral load. No other HIV medications were taken during the study. It is important to remember, however, that current HIV treatment guidelines recommend combination therapy with agents from at least 2 classes of HIV drugs and do not recommend monotherapy (using a single drug to treat HIV infection or AIDS).

In the group receiving the highest dose of PRO 140 (5 mg/kg of body weight), everyone had a strong, fast, and long-lasting drop in viral load that continued up to 3 weeks. Viral load reductions this large have not been reported for a single dose of any other HIV drug. There was also a significant increase in T-cells for individuals receiving the 5 mg/kg dose. After 8 days, there was an average increase of 129 T-cells, and the T-cell levels stayed elevated for 3 weeks after treatment. Patients who received the 5 mg/kg dose still had viral loads well below what they were before they were treated with PRO 140 and the drops lasted for 2 to 3 weeks after starting the drug.

The down side to PRO 140 is that it must be delivered by a health-care professional by intravenous injection. This probably means, however, that it can be given less frequently than most of the other HIV drugs—that is, once a week instead of the usual once or twice a day. This will help patients avoid some of the problems related to taking drugs with or without food, as well as the **interactions** that can result from taking many drugs together. In addition, PRO 140 was generally well tolerated with no serious side effects. Progenics Pharmaceuticals reported that it has developed a version of PRO 140 that can be delivered by **subcutaneous** injection. This delivery method would make it even easier for patients to manage because the subcutaneous version can be self-administered.

Data on another new chemokine antagonist, known as ***vicriviroc*** (SCH 417690), showed a reduction in viral load that was similar to that achieved with maraviroc (Abstract H-1030). Roy Gulick, of Cornell Medical College in New York, said that the 79 patients in the study also had an increase in T-cells that lasted over time. The purpose of the study was to see if patients had a decrease in their viral loads when 30 mg of vicriviroc was added once daily to an optimized background therapy when compared to a control group receiving new optimized background therapy alone. One of the good things about this drug is its once-daily dosing, rather than the twice-daily dosing that is required with maraviroc. Although there is some concern about patients developing cancerous tumors, the researchers are not sure what causes them. It could be the drug itself, or it could be that the patients in the study had weak immune systems so they were more prone to getting sick. Since the patients on maraviroc did not appear to have more cases of cancer, the researchers believe that the tumors that developed during this study are probably related to weak immune systems.

Overall, the biggest concern about the chemokine antagonists is finding out what will happen if someone does not respond to treatment with this class of drugs. Researchers have determined that if a drug that is designed to block the CCR5 receptor does not work for a particular person, he or she will probably also be resistant to drugs that block the CXCR4 receptor, another cell protein that HIV uses to infect T-cells. Even though resistance to this class of drugs may cause an increase in viral load, the T-cell response will still be good enough to protect the body to a certain extent.

Integrase Inhibitors

José Gatell, from the University of Barcelona in Spain, presented the latest information on ***raltegravir*** (Abstract H-713), now known as Isentress™, the first **integrase inhibitor** to be approved by the FDA. It is intended for patients who have taken many HIV drugs and are resistant to most of them. About 178 patients received either a placebo or 1 of 3 doses of raltegravir (200 mg, 300 mg, or 400 mg) twice daily, in combination with opti-

mized background therapy. When the study started, the average viral load was about 50,000 copies, and the T-cell counts were about 200. Data from the ICAAC showed that more than half of the patients had a viral load below detectable levels (less than 50 copies) for 48 weeks. Although about 30% of the patients with resistance to raltegravir also showed resistance to other integrase inhibitors, there was no sign of serious cancerous tumors. *For more information on this drug, see P. 14 in this issue.*

Elvitegravir, another integrase inhibitor that is still in Phase 3 trials, also showed promising results (Abstract H-714). According to Andrew Zolopa, from Stanford University in Stanford, California, 278 patients took 1 of 3 doses of elvitegravir (20 mg, 50 mg, or 125 mg daily) **boosted** with 100 mg twice daily of ritonavir (Norvir®) or a protease inhibitor (PI) also boosted with ritonavir. In addition, all participants took reverse transcriptase inhibitors (commonly known as "nukes"), with or without Fuzeon® (T-20), a fusion (entry) inhibitor that works outside of T-cells to help prevent HIV from infecting cells in the first place. At the start of the study, the 73 patients who received elvitegravir had an average viral load of 80,000 copies and extensive resistance to most of the existing protease inhibitors. Everyone in the study had already taken many HIV drugs and had developed resistance to most of them.

After 24 weeks, elvitegravir combined with ritonavir was actually more effective than the existing protease inhibitors were, bringing viral loads down to about 8,000 copies. As was expected, the best response to the drug was seen in the patients who were taking the highest does of elvitegravir and had less resistance to other drugs—their viral loads dropped to less than 50 copies. The other good news is that elvitegravir can be given once a day in combination with ritonavir, whereas raltegravir must be taken twice a day.

Other Classes with New Drugs

The approval and development of entirely new classes of drugs is a long-awaited boon in the treatment of HIV and AIDS. It offers a new set of options for people who were beginning to run out of them. But equally exciting is the progress that is being made in the existing classes.

One of these is ***etravirine*** (TMC-125), a non-nucleoside reverse transcriptase inhibitor (commonly known as "non-nukes"), which was given to about 1,200 treatment-experi-

enced patients (Abstract H-717). Participants were given either a placebo or a combination of 200 mg of etravirine, twice-daily darunavir (Prezista™), and ritonavir, together with a choice of nukes. In addition, patients were given the option of using Fuzeon. Pedro Cahn, from Buenos Aires, Argentina, reported that at the start of the study, patients had to have a history of resistance to other non-nukes and to protease inhibitors, as well as fairly high viral loads around 100,000 copies and low T-cell counts of about 100. The patients on etravirine had a very good drop in viral load and a small but significant increase in T-cells. The most important news is for the people who are resistant to other non-nukes. The group of patients taking etravirine had viral loads less than 50 copies. Although the increase in T-cell count was only about 20, people in the study appeared to be healthier after taking etravirine, with fewer cases of AIDS-defining illnesses or death. The drug is not approved yet, but is available in expanded access programs.

A new non-nuke, known as ***UK-453***, appears to have very good antiviral activity and can be taken once a day (Abstract F1-945). Pfizer researchers presented data from a study of HIV monotherapy in which 48 participants received 500 mg of UK-453 twice a day or 750 mg once a day. The viral load was dramatically reduced in just 7 days. It is important to remember, however, that current HIV treatment guidelines recommend combination therapy with agents from at least 2 classes of HIV drugs and do not recommend monotherapy.

Researchers from Ardea BioSciences, a company in Costa Mesa, California, presented data on another non-nuke called ***RDEA806*** (Abstract H-1040). The company conducted 2 studies involving 92 healthy adult male volunteers, of which 78 received RDEA806. With doses ranging from 50 mg to 600 mg, the researchers determined that the drug was safe and well-tolerated at all doses without serious side effects. It also succeeded at keeping the viral load down. There are several good features to this drug: it has the potential to be used in patients who have never taken drugs, as well as in those who have undergone treatment before; it was designed to avoid the usual resistance patterns seen with other non-nukes, which could mean that it would take longer for a patient to develop resistance; and, it seems able to stabilize or to decrease **cholesterol** and **triglyceride** levels, conditions that other HIV drugs have often aggravated.

More Bad News about Treatment Interruptions

Heart Disease Risk without HIV Treatment

One study that has stayed in the news is the SMART (**S**trategies for the **M**anagement of

Anti-**R**etroviral **T**herapy) Study. In the June 2007 issue of *HIV Treatment Alerts!*, we reported on surprising results that indicated that delayed or interrupted treatment (drug conservation) caused more than twice the risk of AIDS or death than immediate, continuous treatment (viral suppression). Furthermore, stopping treatment led to more serious illnesses, including liver, kidney, and heart disease. Researchers have continued to explore these findings because new evidence suggests that untreated HIV infection can be a bigger threat to heart health than the high cholesterol that is caused by HIV drugs. New data reported at the ICAAC may finally explain why this is the case (Abstract H-378).

In a study designed to look at the significance of treatment interruption, Pablo Tebas, from the University of Pennsylvania, presented information about the 47 HIV-positive patients who were enrolled in the AIDS Clinical Trials Group (ACTG) study 510. These patients were on stable HIV regimens and had viral loads below 200 copies and T-cell counts above 500 cells. The patients continued their HIV meds with or without interleukine-2 (IL-2), a drug normally used to treat cancer but one that also seems to boost the immune system in people with HIV infection. After 18 weeks, all patients stopped taking their HIV meds until their T-cell counts fell below 350. Various **metabolic** tests, such as measurements of sugar, cholesterol, and triglyceride levels in the blood, were checked frequently in the patients while they remained off treatment. The upside was that after 8 weeks of interrupted treatment, total cholesterol, triglycerides, and "bad" cholesterol (low-density lipoprotein, or LDL) levels went down very quickly. This drop in the levels of artery-clogging, bad cholesterol is good for the heart. Unfortunately, the level of "good" cholesterol (high-density lipoprotein, or HDL), the one that protects a person from heart disease, also dropped. This situation, combined with a jump in viral loads while off HIV meds, may be the reason why the risk of heart disease actually increases. The result is a "washout", meaning that there is no benefit to the **lipid levels** by stopping HIV drugs.

Continuing Problems with Side Effects

Cancer Risks

While the development of new drugs to fight HIV is always exciting, people with HIV infection continue to battle the negative effects of these very strong HIV meds. Numerous reports out of the ICAAC presented updates on the state of controlling treatment side effects.

Researchers from the United States Department of Veterans Affairs compared the medical records of 33,400 HIV-positive and 66,800 HIV-negative veterans to see how many cases of cancer—not related to AIDS or not indicative of an AIDS diagnosis—had occurred during 5 to 6 years of follow-up (Abstract H-1721). They found that the rate for these events in HIV-positive patients was 60% higher than that seen in the HIV-negative individuals. When they looked at which kinds of cancer occurred more often, they found that the most common affected the anus or lungs. Some of these cancer occurrences may be the result of other comorbid conditions, a situation in which 2 diseases occur together, such as HIV infection and heart disease. The high rate of anal cancer is most likely related to human papillomavirus (HPV) infection, whereas lung cancer is probably associated with increased smoking among veterans. Increased cases of liver cancer may be related to having hepatitis B or C together with HIV infection. However, melanoma (an aggressive skin cancer) and Hodgkin's disease (a cancer of the lymph system), which are unrelated to other medical conditions, occurred more often. The important thing to remember is that in most of these cases, the individuals who got cancer tended to have lower T-cell counts than HIV-infected individuals who did not have any cancer.

A group of French researchers looked at a population of more than 1,200 patients who had started taking HIV drugs, including a protease inhibitor, between 1997 and 1999 (Abstract H-1722). The goal was to determine the rate of and risk factors for serious illness or death that was neither related to having AIDS nor attributable to the side effects of HIV drugs. They found that about 23% of the patients had bacterial infections and that about 10% of them had cancerous tumors. Another 10% of patients had **cardiovascular disease**, as well as some psychiatric and neurologic events. Not surprisingly, the researchers found that being older put patients at greater risk of such events. They also found that having hepatitis C was related to an increased risk for these specific events, but this might be because hepatitis C causes liver disease. More importantly, they found that having a T-cell count less than 100 or a viral load greater than 10,000 copies would significantly increase a person's risk for events not related to AIDS or HIV treatment. Taking into account the reports about the increased health risks that occur after stopping HIV therapy, patients should seriously consider whether treatment holidays are worth the risk.

Kidney Risks

We reported in the last issue of *HIV Treatment Alerts!* on the kidney problems experienced by patients taking ***tenofovir*** (Viread®). Knowing about these problems is important because this drug has been used regularly for long periods of time. Two groups of

researchers looked at the problem from a different perspective: finding out to what extent tenofovir affects patients who often are excluded from previous clinical studies because they already had kidney disease. They looked at 2 small groups of patients with kidney problems who were being treated with tenofovir.

Ben Young, from Denver, Colorado, presented data from the HIV Outpatient Study (HOPS), in which they identified 19 patients—6 of whom had previously had kidney disease but whose kidneys were functioning normally when they entered the study, and 13 of whom had confirmed kidney problems (Abstract H-382). In the 13-month follow-up period, 3 of the 6 patients who had previous kidney problems and 2 of the 13 patients who had current problems experienced worsening of their condition. This means that patients who have poor kidney function before they start taking tenofovir will probably have even worse kidney function after they take the drug, thus supporting the finding that tenofovir is associated with an increased risk of kidney disease. What was surprising was that, of the patients with past kidney problems, 50% did *not* experience worsening problems, and that 11 of the 13 patients with current kidney disease actually did *not* get worse. What this suggests overall is that although tenofovir does place these high-risk patients at greater risk for kidney disease when compared to the patients who did not have current kidney problems, it could still be used with appropriate caution and ongoing monitoring in the high-risk patients. In this case, it would provide an additional option for patients with poor kidney function who have become resistant to other drugs.

A University of Maryland group did a similar study of the risks of tenofovir looking at a population of African-Americans who are at higher risk for many of the comorbid conditions associated with kidney disease, like diabetes and hypertension, as well as kidney disease related to HIV (Abstract H-383). They examined 2 populations: 150 people who received a combination of HIV meds that included tenofovir and 68 who received combinations that included abacavir (Ziagen®). The researchers found that there was a reduction in kidney function among those treated with tenofovir when compared to those treated with abacavir. Although most of the problems with kidney function happened very early after starting tenofovir, it seems that there were actually very few cases. In fact, only 4 (3%) out of 149 patients in the

tenofovir group had to discontinue therapy because of worsening kidney function, versus none of the patients in the abacavir group. The trouble, as it turns out, is that there were some differences between the 2 groups at the start of the study. In particular, the people who received tenofovir tended to be a little bit younger, so their kidneys actually functioned somewhat better than the patients in the abacavir group. The message is that although there probably is a negative effect from tenofovir, it tends to be modest and is only seen in a very small number of people. As a result, clinicians can probably continue to use this drug carefully if they closely monitor kidney function in their patients.

Metabolic Problems

Even after 25 years of studying HIV and AIDS, researchers have only a few theories to explain why many patients suffer from **lipodystrophy**. The main theories are that:

- HIV medications, including protease inhibitors, interfere with fat metabolism, causing a buildup of fat around the gut or a loss of fat and muscle in the face and arms and legs. However, some patients who have lipodystrophy have never been on a treatment program that included a PI.

- HIV causes insulin resistance, which interferes with sugar metabolism. People who have insulin resistance (pre-diabetes or diabetes) tend to gain weight because of the disruption in fat and sugar metabolism.

- Lipodystrophy may be just another complication of having HIV infection. Before there were so many drugs to treat HIV infection, people with HIV did not live as long as they do today. Some scientists think that lipodystrophy may simply be a long-term side effect of living with HIV infection for many years.

Many treatment activists have argued that pharmaceutical companies do not want to fund studies that would emphasize or bring to light problems caused by their drugs. On the other hand, drug companies might be interested in conducting research that shows how their product caused fewer problems than a competitor's product. At this year's ICAAC, there was not much new data to report on this subject. However, at the 11th European AIDS Conference in Madrid, Steven Grinspoon, of Harvard Medical School, presented follow-up data (Abstract LBPS7/3) on the second 26 weeks of the data reported at this year's Retrovirus Conference (*HIV Treatment Alerts!*, June 2007).

To date, no treatments have been approved to manage the buildup of fat around the gut that occurs in many HIV-positive people. Studies have shown, however, that taking ***Serostim***® (recombinant human growth hormone) reduces the fat buildup. Unfortunately, Serostim is associated with some notable side effects, including fluid retention and an increased risk of having high blood sugar. In fact, Serostim has been turned down for approval by the FDA for the treatment of

lipodystrophy, although an appeal is pending. Theratechnologies, a company based in Montreal, Canada, has been experimenting with the use of a synthetic growth hormone release factor (GRF), dubbed ***tesamorelin*** (previously known as TH9507), as a treatment for fat buildup. For the first 26 weeks, patients were randomized to receive either daily subcutaneous injections of 2 mg tesamorelin (273 patients) or placebo (137 patients). After 26 weeks, patients receiving tesamorelin were either switched to placebo (50 patients) or continued taking the drug (154 patients). All patients originally randomized to receive placebo were given tesamorelin for the second 26 weeks of the study. Data presented at the Retrovirus Conference showed that patients treated with tesamorelin saw their fat buildup decrease by 15%. In the placebo group, the average drop was only 5% percent.

In the second half of the study, patients treated with tesamorelin for a total of 52 weeks had lost 18% percent of their fat buildup, most of it during the first 26 weeks of treatment. Patients who were treated first with tesamorelin and were then switched to placebo had a much smaller decrease in limb fat of only 2%. Researchers at Theratechnologies suggest that the use of tesamorelin may result in treatment benefits similar to those seen with Serostim but with fewer side effects. They concluded that the safety profile of tesamorelin at 52 weeks is very satisfactory. As for rebounds in limb fat seen in patients who switched from tesamorelin to placebo, it appears that continuous treatment with the drug will likely be required to maintain fat loss.

The other side of the lipodystrophy problem is preventing limb fat loss. Gilead Sciences is conducting a clinical trial (Study 903) that will continue for almost 7 years with participants from Argentina, Brazil, and the Dominican Republic (Abstract H-364). The purpose is to determine if HIV treatment that includes tenofovir is better at preventing limb fat loss than combinations containing stavudine (d4T, Zerit®). The first phase, which is now completed, lasted 144 weeks and compared d4T to tenofovir, in addition to 3TC (lamivudine, Epivir®) and efavirenz (Sustiva®). The current phase of the study is looking at 2 groups of patients: those who switched from d4T to tenofovir versus those who have continued to use tenofovir since the beginning of the study.

At the time of the switch in meds, the group that switched consisted of 85 participants

with an average T-cell count of 650 and controlled viral loads (less than 400 copies). All of the patients still under follow-up have maintained viral loads of less than 400 copies. Data presented at last year's Eighth International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV in San Francisco showed that 2 years after switching from d4T to tenofovir, limb fat levels increased in those patients who switched their meds. No significant changes in limb fat had been detected in the group continuing to take tenofovir. The researchers concluded that switching d4T to tenofovir, as part of a once-daily treatment plan with 3TC and efavirenz, resulted in significant improvements in limb fat and lipid levels, suggesting that tenofovir is a better treatment option for individuals suffering from this problem.

Drug Resistance

Some of the most interesting data about drug resistance came at the end of the ICAAC, when researchers from Tibotec Inc. presented 48-week results from ARTEMIS (Abstract 718b). This study compared a once-daily dose of ***darunavir*** plus ritonavir to once-daily or twice-daily ***Kaletra***® (lopinavir/ritonavir) in 689 patients taking HIV meds for the first time; the drug was originally approved for patients who have taken many HIV meds. All patients in the study also took ***Truvada***® (tenofovir plus emtricitabine). About 36% of the patients in both study groups began treatment with viral loads higher than 100,000 copies. Results indicate that among this group of patients, 84% of those treated with darunavir had viral loads below 50 copies after 48 weeks, whereas 78% of those treated with Kaletra had a similar reduction. This suggests that once-daily ritonavir-boosted darunavir works equally or better than Kaletra alone at reducing viral loads in patients who have a viral load higher than 100,000.

Although the researchers did not intend to compare once-daily to twice-daily dosing, they discovered that once-daily darunavir/ritonavir may have an advantage over once-daily Kaletra. An 800 mg dose of darunavir was given with a 100 mg dose of Norvir once-daily, whereas Kaletra was given at either of the 2 standard doses (400/100 mg twice daily or 800/200 mg once daily). When compared with the 84% of darunavir-treated patients who had viral loads below 50 copies after 48 weeks, only 71% of the patients treated with once-daily Kaletra achieved similar results. While it is too soon to conclude that once-daily darunavir/ritonavir is superior to once-daily Kaletra, especially because only 15% of patients in the Kaletra group were taking the once-daily dose, this study does suggest that it is fine to give Kaletra once daily to patients who have such high viral loads. The advantage to Kaletra is that both drugs are combined in one pill, a treatment schedule that appeals to many patients.

NEWDRUGPROFILE:

Raltegravir (Isentress™)

Raltegravir tablets are pink, film-coated and oval-shaped; "227" is imprinted on one side.

Background and description. Raltegravir is an HIV integrase inhibitor; it is the first drug in its class. In October 2007, the United States Food and Drug Administration approved raltegravir for use in HIV-infected, treatment-experienced adults whose virus is resistant to other anti-HIV medicines. Merck and Co. sells the drug under the brand name Isentress.

Raltegravir works by blocking the insertion of HIV DNA into the host cell genome.

Dose. The standard dose is 400 mg by mouth, twice daily.

Food restrictions. None. You may take raltegravir with or without food.

Missed dose. If you miss a dose, take it as soon as you remember, unless it's almost time for your next dose. In that case, skip the missed dose and start back on your regular schedule. Don't try to make up for a missed dose by double dosing.

Storage. Store raltegravir tablets at room temperature (66-77°F).

Patient assistance. Merck & Co. provides raltegravir free of charge to those who qualify. For more information, **call 1-800-850-3430**.

Side effects. The data from 2 studies suggest that raltegravir is well-tolerated. In fact, the research participants who took a placebo were more likely than participants who took raltegravir to complain of side effects. In these studies, the most commonly reported side effects were diarrhea, nausea, headache, and fever.

Drug interactions. Because of the way it's metabolized, raltegravir doesn't have as many drug interactions as other anti-HIV treatments do. But certain medications—including rifampin, a drug for tuberculosis—reduce the blood level of raltegravir. To avoid dangerous drug interactions, make sure all of your health-care providers know the medications you're taking.

Efficacy. In two studies of heavily treated patients with advanced HIV infection, raltegravir demonstrated potency equal to the protease inhibitors. After 6 months of treatment with raltegravir, the average viral load reduction was 1.85 logs; the average T-cell increase was 89 cells. On average, these patients had used anti-HIV therapy for 10 years; almost 76% of them pushed their viral loads below 400 copies, and nearly 63% reached viral loads below 50 copies. All patients took combination therapy. More than a third took Fuzeon, which is given by injection. Your doctor may order special tests to decide what other drugs to combine with raltegravir.

DEFINITIONS
definitions

Boost (boosted)**:** to elevate levels of a drug in the body.

Cardiovascular: relating to the heart and blood vessels.

Cholesterol: a fat-like substance that occurs naturally in all parts of the body and is made by the liver. Too much cholesterol in the body increases a person's risk of getting heart disease.

Chemokine antagonists: also known as CCR5, short for chemokine receptor 5. This new class of antiretroviral drugs blocks HIV from attaching to the CCR5 receptor on the T-cell, making it hard for the virus to enter T-cells.

Integrase inhibitors: a new class of antiretroviral drugs that blocks the action of integrase, an enzyme that inserts genetic material from the virus into a person's cells.

Intravenous: injected into a vein.

Lipid levels: fats and fatty substances used as a source of energy in the body. Lipids include cholesterol, triglycerides, high-density lipoprotein (HDL; "good" cholesterol), and low-density lipoprotein (LDL; "bad" cholesterol).

Lipodystrophy: changes in body fat, such as loss of fat in the arms and legs and accumulation of fat in the gut or at the back of the neck.

Metabolic (metabolism)**:** chemical reactions in the body that are part of life; for example, turning food into energy or breathing in oxygen and breathing out carbon dioxide.

Randomized: to select by chance, as in a sample or experiment.

Opportunistic infection: a disease or infection caused by an organism that is usually harmless but becomes activated when a person's immune system is weakened or damaged.

Optimized background therapy: the combination of HIV meds most likely to increase T-cell count and decrease viral load based on history of HIV meds and drug resistance testing.

Placebo: a pill or substance that has no effect on the body, such as a sugar pill. It is often compared to a real medication to see what the real effect of the medication might be.

Resistance (resistant)**:** a genetic change that allows HIV to reproduce itself in the presence of an HIV medication.

Subcutaneous: injected under the skin.

Toxicity: the degree to which a substance is poisonous or dangerous.

Triglycerides: a type of fat the body uses to store energy.

communityspotlight

The Houston Buyers Club (HBC)

is a non-profit, 501(c)3 organization that has been helping people living with chronic illness to manage the symptoms of their conditions, as well as many of the side effects associated with the medications used to treat these illnesses. Founded in 1996, the HBC aims to improve the quality of life for patients by providing affordable nutritional supplements at a reduced cost to people living with AIDS and other chronic illnesses, such as diabetes, hepatitis A, and cancer. They also offer a nutritional supplement grant program, dietitian services, and peer education. HBC has produced a comprehensive Side Effects Guide that physicians and patients can use to reduce and eliminate many of the common side effects caused by disease or the medications used to treat the disease.

The HBC is open to the public and offers a wide variety of health and dietary supplements in its storefront space.

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