# STRATEGIES FOR HIV THERAPY

◼

information to consider when deciding to use therapy

Most people living with HIV will start taking therapy at some point to help control their HIV infection. The goal of therapy is to slow or stop HIV from reproducing. This, in turn, helps to slow or stop the progression of HIV disease as well as the destruction of the immune system. While other ways of treating HIV disease have been studied, so far only HIV therapy has shown to slow disease progression and extend life.
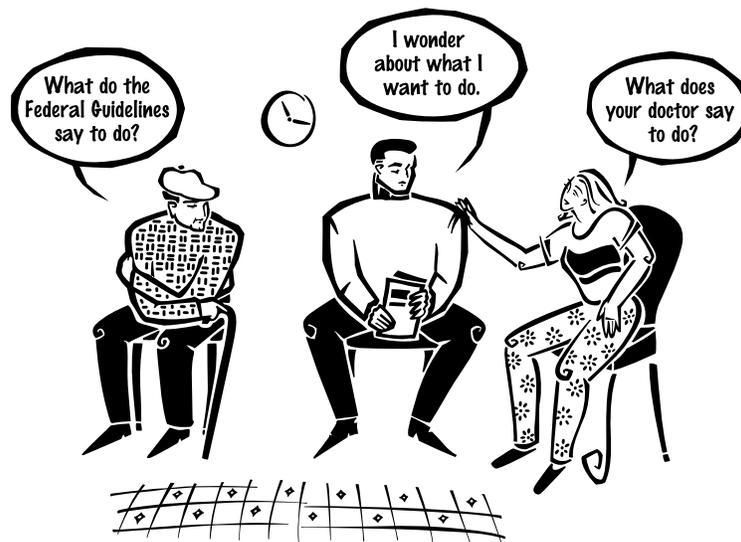
While trying to understand and make decisions about using HIV therapy can be an overwhelming process, it isn't insurmountable. With the support of your doctor and reliable information, it's possible to devise a wise HIV strategy that suits your situation. This includes balancing the benefits, risks and limitations of the current HIV drugs along with the prospects offered by novel approaches and newer drugs.

This publication provides information on making these types of decisions. It offers a range of issues that you may encounter when deciding what's necessary and important for your health. It's intended to assist you and your doctor making the best possible decisions about using HIV therapy in adults and adolescents.

the goals of hiv therapy

HIV therapy should:

- **PROLONG** life and improve quality of life;

- **SUPPRESS** HIV levels (viral load) below the limit of detection (<50 copies HIV RNA), or as low as possible for as long as possible;

- **OPTIMIZE** and extend the use of current therapy; and

- **MINIMIZE** drug toxicity, and manage side effects and drug interactions.

What is HIV and HIV disease?

HIV, or human immunodeficiency virus, infects and takes over certain cells of your immune system, which is your body's defense for fighting infections and diseases. Once these cells are infected, HIV uses them to make new copies of itself (replication) and then go on to infect other cells. Infected cells function poorly and die prematurely, which in turn weakens the immune system. This allows *opportunistic infections* to develop, which take the opportunity to thrive while your immune system is damaged.

HIV disease is a broad term that refers to having HIV infection, from the earliest stage right after infection to later stages of disease. AIDS (*acquired immune deficiency syndrome*) occurs later in HIV disease when the immune system has become severely weakened. An AIDS diagnosis depends upon the state of your immune health or an AIDS-defining condition(s).

Once HIV was identified as the cause of AIDS, stopping or slowing its replication became a major goal. Significant progress has been made over the past 20 years, especially with the advent of potent HIV drugs and combination therapy. Though these drugs do not eliminate HIV, they've made it possible to develop long-term strategies for managing HIV disease.

It's important to remember that people can live a long time, without symptoms of HIV disease. Still, some questions remain around when to start, when to switch or how best to combine HIV drugs. Making wise decisions about how best to use therapy requires understanding the risks and benefits of HIV drugs, discussing these issues with an informed doctor, and properly using various lab tests.

The challenges of therapy

Unless HIV replication is controlled, trying to rebuild immune health will ultimately fail — at least most of the time. Although using therapy hinders HIV from replicating, it does not eradicate the virus from your body. Many scientists fear that it's not possible to fully eliminate it. Others don't share this pessimism, pointing to newer and better drugs as well as an ever-growing understanding of HIV disease and its effects on the immune system.

Over time, HIV can mutate or change enough so that it's no longer fully blocked by these drugs. This process is called viral resistance and it can happen to some degree with all HIV drugs. However, keeping HIV under control lengthens a person's life, and it may be possible — with truly effective therapy — to live out a normal lifespan despite HIV.

Abundant evidence shows that using potent HIV therapy has dramatically lowered death rates. It has also increased life and quality of life for people living with HIV. However, the drugs are not without their risks of side effects. When deciding on therapy, the possible short- and long-term side effects must be weighed against possible short- and long-term benefits, particularly as you consider when to start.

There's little research on using HIV drugs in the earlier stages of HIV disease. Many, if not most, people don't have to decide this immediately after learning they have HIV. Assessing your risk of disease progression and making decisions that you feel comfortable with are important parts of building a successful long-term HIV strategy.

Why use anti-HIV therapy?

When you're first infected with HIV, high levels of HIV replication often occur with flu-like symptoms and a decline in the number of CD4+ cells. CD4s are key cells in your immune system that maintain and direct responses against disease. They are also commonly used to measure your immune health.

Without using HIV therapy, your immune system dramatically but incompletely suppresses the virus. In most cases, CD4s return partially toward normal levels and people usually regain good health for many years. Yet, during this time an aggressive battle is waged daily between your immune system and HIV. Over time, the immune system becomes overwhelmed by HIV's rapid and constant activity.

The relationship between your HIV levels and risk of disease progression is complicated. An influential study by John Mellors found a solid relationship between HIV levels and risk of death over time. Other research suggests that CD4+ counts better predict the risk of disease progression. However, it is well established that reducing HIV levels typically leads to a stronger immune system and better health.

Considering these points, it makes sense to slow down or stop HIV replication as much and for as long as possible. All approved HIV drugs significantly reduce HIV levels, and they almost always cause some rise in CD4+ counts. Lower viral loads and higher CD4+ counts indicate some improvement in your immune system.

the basic message from project inform

➤ Learn about HIV testing options and choose one that fits your needs! Be sure your privacy is protected!

➤ If you're positive, don't panic. If you make your health a priority, chances are you will be reasonably healthy for many years.

➤ Learn about your healthcare options and local support services.

➤ Get a complete physical and blood tests for CD4+ cell count & HIV level. Repeat quarterly and watch for trends. Women should get GYN exams and Pap tests every six months, more often if abnormal.

➤ Work with a doctor to develop a long-term strategy for managing HIV disease.

➤ If the CD4+ cell count is below 350 or falling rapidly, consider starting anti-HIV therapy. Test at least twice before taking action.

➤ If therapy fails to reduce your HIV level below the "limit of detection" or below 5,000 copies within 3–6 months, consider a different or more aggressive therapy.

➤ If the CD4+ count trend stays below 300, consider treatment for preventing PCP. If it stays below 200, start treatment for preventing PCP (if you haven't already done so) and reconsider anti-HIV therapy if not on one. Learn about drug interactions and preventive treatments for opportunistic infections.

➤ If you started preventive therapies and your CD4+ cell count rises in response to anti-HIV therapy, ask your doctor whether it might be safe to stop certain preventive therapies.

➤ If your CD4+ cell count stays below 75, consider more frequent blood work—perhaps even monthly. Consider therapies for preventing MAC/MAI and CMV.

➤ Regularly seek support for your personal, spiritual and emotional needs. It takes more than medicines to keep you well.

When should I start treatment?

It remains unclear when the best time to start therapy is. The "best" time for one person may not be the "best" time for another. There's also much debate about which drugs to start with and in what combinations. Several factors — including HIV levels, CD4+ counts as well as how you feel about therapy — are important to consider when deciding if and when therapy is right for you.

Many questions can also be considered when making these decisions. Should treatment be used immediately when you first learn you have HIV? Should therapy be saved until changes occur in your immune health? Should it be saved until there's a higher viral load, or until symptoms of HIV develop? For more information, read Project Inform's publication, *Strategies for When to Start HIV Therapy*, available at 1-800-822-7422 or *www.projectinform.org*.

In deciding when to start, switch or change HIV therapy, three medical factors are generally considered:

❯ What's happening with measures of your immune health (particularly CD4+ counts)?

❯ What's happening with your general health, like symptoms of HIV disease or recurrent conditions despite treatment?

❯ What's happening with your HIV levels?

Deciding to begin treatment is not solely a medical matter. Other factors must be considered, including:

❯ Your feelings about therapy;

❯ Your readiness and willingness to take therapy, including taking it as prescribed;

❯ The impact that therapy may have on your quality of life;

❯ Possible side effects;

❯ How long therapy can last, and whether or not there will be new and better drugs to replace them if or when they fail; and,

❯ Your risk of disease progression in the short-, middle-, and long-term.

So, should I start because of my...
hiv level?
cd4+ cells?
general health?

When is the right time to start?

Some believe there can be no single, right answer to the question of when to start. Some researchers and doctors believe that nearly everyone with HIV — regardless of their CD4+ counts, viral loads or symptoms — should be treated. Some believe people should start therapy only when their CD4+ counts consistently read below 350. Others believe that only people with symptoms of HIV disease should consider therapy.

One note of agreement is that most researchers and doctors believe that the decision to start should be guided by both CD4+ cell counts and overall general health. Increasingly, information suggests that CD4+ counts provide the most accurate tool to monitor the risk of HIV disease progression.

The most commonly used viral load tests are Roche's RT-PCR (polymerase chain reaction test, called Amplicor HIV Monitor Test), Chiron's bDNA (branch DNA test, called Quantiplex) and Organon Teknika's NASBA (nucleic acid sequence based amplification test, called NucliSens). When possible, it's best to use the same lab and same test every time. For example, RT-PCR results are consistently higher than those obtained with bDNA. Similarly, different labs might get somewhat different results when running a CD4+ count.

For more information on blood work, read Project Inform's publications, *Blood work: Two common tests to use* and *Blood work: A complete guide for monitoring HIV*, available at 1-800-822-7422 or *www.projectinform.org*.

Quality of life issues

Your ability to tolerate side effects, drug interactions and the demands of a regimen can be as important as the potency of a drug. If you can't take a drug as prescribed, its potency is irrelevant. Not adhering to therapy contributes to developing drug resistance, and developing resistance to one drug might lead to cross-resistance to other drugs in the same class.

When choosing therapy, consider the daily pill count of everything you take. These include the HIV drugs, drugs to prevent and treat other infections or conditions, supplements, etc. Consider when they have to be taken and whether or not they can be taken with other medicines or food. It's easiest to combine drugs that require similar conditions, such as with or without food. Otherwise, one's life can become dominated by drug schedules.

It's also best to avoid mixing drugs with similar side effects, though sometimes that is impossible. It's critical to learn about the possible side effects of each drug that you take as well as possible drug interactions before mixing them together. To help better understand these issues, read Project Inform's publication, *Dealing with Drug Side Effects*, as well as materials on each HIV drug, available at 1-800-822-7422 or *www.projectinform.org*.

Not everyone experiences side effects. Learning about possible side effects and drug interactions before starting therapy allows you to be aware of what to check for and to consider ways to prevent or manage them, before they happen. The more informed you

are, the less likely you will come across severe or life-threatening side effects. Also, the more prepared you are, the less likely that side effects and drug interactions will interfere with adhering to your regimen.

One side effect of particular concern is changes in body composition and metabolism, generally called *lipodystrophy*. They include fat accumulation (*lipohypertrophy*) and/or fat loss (*lipoatrophy*) and/or changes in lab values of fats (*dyslipidemia*) or sugars/insulin (*diabetes*). Some HIV drugs contribute to these conditions more than others.

Another condition, impacting the energy source inside cells (mitochondrial toxicity), is particularly associated with using NRTIs (see chart on page 8). Also, reports of people experiencing bone loss are increasing. All of these conditions may result from long-term use of HIV therapy. For more information, read Project Inform's publications, *Bone Health and HIV Disease* and *Mitochondrial Damage*, available at 1-800-822-7422 or *www.projectinform.org*.

viral load and women

Several studies suggest that women generally have lower HIV levels than men at the same CD4+ cell counts. Some suggest that these differences decrease or disappear after the first five years of HIV infection.

The current Federal Guidelines recognize that HIV levels may be somewhat lower in women, but they don't alter the goals of HIV therapy — to lower HIV levels to as low as possible and improve CD4+ counts and overall general health. They conclude that these data should not affect using therapy in women or in men.

The US Department of Health and Human Services issues *Guidelines for the Use of Antiretroviral Agents in the Treatment of HIV-Infected Adults and Adolescents*. These are summarized in the table on page 11.

The Guidelines describe the recommendations of researchers, and point out that people with HIV and their doctors must consider many other factors, like a person's readiness to start treatment or concerns about long-term toxicity and drug resistance.

Points for people to think about for people who are considering HIV therapy

There are many issues to consider and discuss with your doctor before starting HIV therapy. The following are ones that you may want to consider if you're starting therapy for the first time (*first line therapy*) or are switching therapy (*second line* or *third line therapy*).

1 Reducing HIV levels as low as possible, preferably below the level of detection, should be an important goal of therapy.

Therapy that has a larger, more consistent and longer lasting effect in reducing HIV levels and increasing CD4+ counts is more likely to produce longer lasting health and survival. People with HIV levels below the limit of detection have much longer lasting responses to HIV therapy than people with consistently detectable levels. When therapy fails to reduce viral loads to undetectable levels, it's usually a sign that it will eventually fail. However, studies show that an occasional "blip" in viral load (a detectable reading every now and then) is not a major concern. Trends over time are more important than a single test result.

Today, viral load tests measure reliably down to 40 or 50 copies. Some older tests still in use measure down to 400 copies. Numbers below this are considered undetectable. Many researchers and doctors believe that people unable to reach undetectable levels after six months on therapy should consider either switching to a new regimen or, if HIV levels are detectable but remain very low (such as below 1,000), adding another drug. Others believe it may be okay for a person with few options to continue using a regimen if it's controlling HIV levels at a low yet detectable level (such as below 5,000). While studies show that reaching "undetectable" viral load is best, the cost of side effects or the complexity of a regimen needed to reach this goal may not be realistic for everyone.

2 There may be some degree of cross-resistance among the drugs in the same class.

Resistance to a drug occurs when HIV changes itself so that it's no longer fully affected by the drug. Cross-resistance occurs when resistance to one drug causes resistance to other drugs in the same class. Resistance usually occurs when the drugs being used are not potent enough to fully stop HIV replication or when the drugs are not taken as prescribed.

For instance, someone with resistance to one of the NNRTI drugs is almost certainly going to be cross-resistant with most of the other NNRTIs (see *Drug ID Chart* on page 8). What this means is that once resistance to one NNRTI develops, most of the other drugs in this class are less effective, and possibly wholly ineffective.

3 Successful long-term use of therapies is more important than short-term gains.

It's possible to get short-term benefits at the cost of wasting potential long-term benefits. An example of this would be starting a two-drug NRTI* regimen in a person with high HIV levels (above 100,000). Studies show that resistance can develop within weeks to months after starting a two-drug NRTI regimen. This may impact the usefulness of other similar drugs as well as eliminating options for future therapies.

* Note: NRTIs are a class of anti-HIV drugs. See the drug chart, page 8.

4 Should I get a resistance test?

Studies show that people who choose therapy based on resistance test results along with their treatment history have longer lasting responses to HIV therapy compared to those who didn't get them before making decisions. Some researchers propose that people get resistance tests before they start HIV therapy for the first time as well as before switching to a new regimen.

In order to run a resistance test, you must have an HIV level above 1,000. Also, resistance tests are likely most reliable when done while someone is on HIV therapy.

5

Therapy that is only partly effective speeds the development of viral resistance.

If an HIV drug reduces viral load yet allows a measurable level of viral activity (measurable viral load), the HIV that's still present is capable of mutating and developing resistance to that drug. When a three-drug regimen doesn't quite succeed in stopping measurable activity, many researchers believe it may be wise to either change two of the drugs or perhaps add a fourth.

It makes sense to try and fully suppress viral replication if this can be done with a reasonable quality of life. When this cannot be achieved, people should realize they can still benefit from therapy and that long-term solutions may become apparent when other drugs become available. Again, using resistance tests may help guide which drugs are not working or which may be useful to add to a regimen.

6

Learn about drug interactions.

Given the number of drugs available to treat HIV and prevent or treat opportunistic infections and other conditions, the potential for drug interactions increases. Not only does each drug have its own possible side effects, it may also increase or decrease the benefit of other drugs. Drug interactions are not always considered when creating a treatment strategy, but they can play a major role in its success. Make sure your health provider knows about all the drugs and supplements you take, including experimental and over-the-counter products.

7

Using a drug exactly as prescribed is critical to success.

Using an inadequate dose, reducing the dose below prescribed levels, or failing to take it at regular intervals increases the risk of resistance. If side effects develop, it's often better to try to overcome them than to immediately change your regimen. If they're not manageable, it's better to temporarily stop all the drugs rather than reduce their doses, and try to solve the problem with your doctor's guidance. The fastest way to develop resistance is to use HIV drugs at inadequate or inconsistent doses.

8

Stopping and starting a regimen often (like on a weekly or even bi-weekly basis) will likely lead to an increased risk of drug resistance.

A structured treatment interruption (STI), as discussed later, may include stopping therapy for two weeks or longer, then restarting it for some period of time. It's important for people considering an STI to be closely checked for HIV levels and CD4+ counts. Many studies show that some people experience a dramatic increase in HIV levels and decrease in CD4s. For more information, read Project Inform's publication, *Strategies for Attempting Structured Treatment Interruptions*.

9

If you need to interrupt therapy, it's best to stop all drugs at the same time (except Viramune and Sustiva) rather than just stopping one drug.

People may need to stop taking their meds for many reasons, including side effects, drug interactions, pregnancy or their drug supply runs out. Stopping HIV drugs, if they're all stopped at the same time, is unlikely to increase drug resistance. Because Viramune (nevirapine) and Sustiva (efavirenz) remain in the body longer than any other HIV drug, they should be stopped at least two or three days and possibly up to two weeks before stopping the others. Otherwise, there's an increased risk of developing resistance to them.

10

People considering a vacation away from home should wait until they return before starting a new drug regimen.

When side effects occur, they often happen within the first 2–4 weeks after starting a new regimen. Many resolve over time as your body adjusts. Some, but not all, people experience mild-to-moderate side effects. A smaller percentage face moderate-to-severe side effects. People should avoid starting a new regimen right before going out of town on vacation or before engaging in major life experiences, like moving or starting a new job. In the unlikely event of serious side effects, it's better to be closer to your doctor.

how will I know if my treatment is working?

One goal of HIV therapy is to reduce HIV levels below the limit of detection (<50 copies) with current viral load tests. However, not everyone can bring their levels to below 50 or even 5,000. For these people the minimum change that shows their therapies are active is a 1 log (90%) reduction. People with lower CD4+ counts and high viral loads may find that their HIV levels drop slowly over time, while people who are healthier are likely to see more immediate responses to therapy.

Pregnant women and therapy

In general, the guidelines for treating pregnant women are the same as for treating non-pregnant adults. The decisions to start, change or add HIV drugs should be based on CD4+ counts and disease stage. The strategies presented in this publication are all valid for pregnant women. The Federal Guidelines recommend that women get the most effective HIV therapy regardless of pregnancy status.

However, how therapy affects an infant or unborn child is not wholly known. Therefore, deciding to use HIV therapy during pregnancy should be made by the woman considering the known and unknown benefits and risks to her and her child. Long-term follow-up is recommended for all infants born to women taking HIV therapy during their pregnancies. Some drugs are not recommended because they cause birth defects either in humans or animals, called Category C and D drugs.

Women in their first trimester (14 weeks) who don't take HIV therapy may decide to delay therapy until after 10–12 weeks because of the possible risks to the developing fetus during that time. However, if a woman's health warrants starting therapy sooner, most would recommend starting it regardless of how far along a woman is.

A woman already on therapy may consider temporarily stopping it until after her first trimester. While there are no clear data on how HIV drugs affect a developing fetus, most doctors recommend staying on a potent regimen regardless of how far along she is in her pregnancy. Stopping or delaying therapy may increase HIV levels — possibly increasing her risk of disease progression as well as the risk of passing HIV onto her child.

Nevertheless, if a woman decides to stop her therapy, all drugs (except Viramune) should be stopped at the same time to prevent drug resistance. Similarly, they should be restarted at the same time. Using Sustiva is strongly discouraged, especially during the first trimester, due to possible harmful effects on the unborn child. Viracept (nelfinavir) is also not recommended. For more information, read Project Inform's publication, *Pregnancy and HIV*, available at 1-800-822-7422 or *www.projectinform.org*.

drug i.d. chart

TRADE NAME	GENERIC NAME
Protease inhibitor	
Agenerase	amprenavir
Aptivus	tipranavir
Crixivan	indinavir
Invirase	saquinavir
Kaletra	lopinavir+ritonavir
Lexiva	fosamprenavir
Norvir	ritonavir
Prezista	darunavir
Reyataz	atazanavir
Viracept	nelfinavir
Nucleoside (NRTI) and nucleotide (NtRTI) analogue reverse transcriptase inhibitor	
Combivir	3TC+AZT
Emtriva	emtricitabine (FTC)
Epivir	lamivudine (3TC)
Epzicom	3TC+abacavir
Retrovir	zidovudine (AZT)
Trizivir	3TC+AZT+abacavir
Truvada	FTC+tenofovir
Videx	didanosine (ddI)
Videx EC	didanosine enteric-coated (ddI EC)
Viread	tenofovir
Zerit	stavudine (d4T)
Ziagen	abacavir
Non-nucleoside reverse transcriptase inhibitor (NNRTI)	
Intelence	etravirine
Rescriptor	delavirdine
Sustiva	efavirenz
Viramune	nevirapine
NRTI + NNRTI	
Atripla	emtricitabine + efavirenz + tenofovir
Entry inhibitor	
Fuzeon	enfuvirtide (T20)
Selzentry	maraviroc
Integrase inhibitor	
Isentress	raltegravir

When is it time to change therapy?

People might change therapy when:

❯ HIV levels become detectable after being undetectable;

❯ HIV levels remain detectable after 4–6 months of starting therapy;

❯ Continued decreases in CD4+ cell counts;

❯ Intolerable side effects occur;

❯ Adherence is poor;

❯ There is less than a 0.5–0.75 log (3- to 6-fold) reduction in HIV levels after four weeks or less than 1.0 log after eight weeks of starting therapy (as noted above, however, for people who start HIV therapy when their CD4+ counts are low and HIV levels are high, it may take longer to realize the effectiveness of a regimen); or

❯ Symptoms of HIV disease occur.

A common infection such as the flu, or even a vaccine shot, can increase HIV levels temporarily. (A flu vaccine can increase HIV levels for up to two months, but they usually fall back to pre-vaccine levels without changing HIV therapy.) Before making a dramatic adjustment in your regimen, factor in how other health issues may be affecting the viral load test results. If possible, wait and get another test before making decisions. The decision to switch or add therapies should be based on at least two viral load tests and/or two CD4+ counts spaced at least two weeks apart, as well as other factors like the readiness to switch and commit to a new regimen.

Write down a list of questions and concerns that you may have for your doctor. It's also helpful to discuss your feelings about taking therapy, especially for the first time. Some of those questions may include:

❯ How do I know whether I'm ready to start therapy?

❯ What I think will happen to me after I start therapy is …

❯ What will happen if I don't start therapy?

❯ Is it possible for me to wait?

❯ How I feel about starting therapy is …

It's probably helpful to keep a list of other questions you may have. Some of these may include:

❯ How potent is this regimen?

❯ What are the side effects of the various drugs, and how often do they occur?

❯ Is there anything I need to do if side effects occur?

❯ How do I monitor for these side effects? Are there things I can do to reduce the risk of getting them?

❯ How often do I need to come in to check and see if my therapy is working?

❯ How often should I take these drugs?

❯ What doses should I take?

❯ Do any of these drugs require a dose change based on my weight or liver or kidney functions?

❯ Are there any interactions between these drugs and other drugs, herbs, vitamins or supplements that I take?

Other questions for people who may also have hepatitis B or C may include:

• Will these drugs affect my liver?

• Are any of these drugs active against my hepatitis?

• Should I treat the hepatitis as well as the HIV?

• Will these HIV drugs interact with my therapies for hepatitis?

Commentary

In addition to issues like your overall general health and quality of life, both CD4+ counts and viral load must be considered when making decisions about starting or switching HIV therapy. Most studies show a direct inverse correlation (when one goes down the other goes up) between viral load and CD4+ counts as more HIV means more CD4s are being infected and destroyed.

Some people, despite substantial decreases in their HIV levels, may continue to experience a decline in their CD4+ counts. In these cases, it's important for doctors to conduct a more extensive diagnosis to see if some other condition is affecting CD4+ counts, such as common or even not so common infections.

It is usually best to start two or more new drugs at the same time. This is readily done for people starting first line therapy but far more difficult for those who have used many other HIV drugs. Your current regimen can sometimes be juggled to get the desired results. For some, this may be impossible.

Everyone does not have access to the same treatments, and people respond differently to individual drugs. Options for treating HIV disease include approved HIV drugs and combinations, experimental drugs gotten through studies or access programs, and other unapproved drugs. Consult with your health provider about how to access the full range of options.

For some people, the best choice may sometimes be to delay using new HIV drugs until enough new drugs are available to start an ideal combination (e.g. at least two drugs never used before by the person). The pace of new drug development is never wholly predictable, which makes this strategy difficult. Working with an experienced doctor who continues to learn from new research is key.

This shift toward long-term thinking is the true hallmark in this third decade of treating HIV. It must become a part of everyone's thinking. The alternative is perpetuating the short-term benefits and long-term failures that were qualities of treating HIV disease earlier in the epidemic.

All of this underscores the fact that people who get medical care from doctors with a great deal of experience in treating HIV disease live longer than those with less experienced ones. HIV is both complicated and extensively studied. A doctor who sees many people with HIV is more likely to understand these complexities and follow the heavy volume of research. Whatever strategy a person chooses, it should begin with finding an experienced doctor who is wise enough to continue studying and learning from new developments in HIV research..

federal recommendations for first line therapy (updated january 2008)

class	preferred	alternative	not recommended
NRTI			
	Truvada	Combivir	d4T
	Epzicom	ddI + 3TC or FTC	
NNRTI			
	Sustiva	Viramune	Rescriptor
			Intelence
Protease inhibitor			
	Reyataz—boosted	Reyataz—unboosted	Invirase—unboosted
	Lexiva—boosted (2x/day)	Lexiva—unboosted	Viracept
	Kaletra (2x/day)	Lexiva—boosted (1x/day)	Aptivus
		Kaletra (1x/day)	Prezista
		Invirase—boosted	

federal | recommendations for when to start therapy

► ARV treatment should be started in anyone with a history of an AIDS-defining illness or before CD4 count falls below 350.

► ARV treatment is recommended regardless of CD4 count for:
  • Pregnant women
  • People with HIV Associated Nephropathy (HIVAN)
  • People co-infected with Hepatitis B Virus (HBV) for whom treatment of HBV is warranted

► The risk of death or serious illness in people with CD4 counts above 350 is low, so any benefit from starting treatment at high CD4 counts is likely to be small.

► There are data — for example the ATHENA cohort — that show that people who start HIV treatment with CD4 counts above 350 are more likely to achieve and maintain CD4 counts above 800.

► Similarly, in the Johns Hopkins Cohort people who started treatment with CD4s below 350 were less likely to achieve and maintain CD4 counts above 500.

► Early HIV treatment has the potential to reduce HIV transmission rates.

► Factors weighing against early treatment would be:
  • the necessity of life-long treatment,
  • the lack of long-term data on most HIV drugs,
  • the potential for developing drug resistance, and
  • the interference with quality of life.

PUBLICATIONS THAT MAY HELP

Project Inform has many publications that can assist you and your doctor to make informed decisions about your therapy and health. You can call the toll-free National HIV/AIDS Treatment Hotline at 1-800-822-7422 for a copy or go to *www.projectinform.org*.

Strategies for improving your immune health	Day one: After you've tested positive
Strategies for maintaining your general health	Dealing with drug side effects
Strategies for managing opportunistic infections	Lipodystrophy
Strategies for when to start HIV therapy	Making decisions about therapy
Adherence: Keeping up with your meds	Mitochondrial damage and lactic acidosis
Blood work: A complete guide for monitoring HIV	Personal tracking charts
Blood work: Two common tests to use	Positive? How are you feeling?
Building a cooperative doctor/patient relationship	Individual HIV drug publications

Chart of the risk of progression to AIDS-defining illness

Some reports show that women progress to HIV disease at a lower viral load than men. While these data do not currently warrant a new standard of care for women with HIV, women and their doctors should be aware of these reports as they may support starting or switching therapy at lower HIV levels than what is currently recommended.

By contrast, CD4+ counts — which provide useful measures for the risk of HIV disease progression — are not influenced by sex.

For more information on this issue, call Project Inform's toll-free hotline at 1-800-822-7422. The chart below presents information on viral load and CD4+ lymphocytes as predictors of HIV-1 infection.

Risk of progression to AIDS-defining illness in a cohort of gay men predicted by baseline cd4+ cell count and viral load[*]

CD4+ cell count ≤ 200 and HIV levels[†] of …

bDNA		RT-PCR		Percent of AIDS-defining illness[‡]			
				n	3 years	6 years	9 years
≤	500	≤	1,500	0[§]	—	—	—
501 –	3,000	1,501 –	7,000	3[§]	—	—	—
3,001 –	10,000	7,001 –	20,000	7	14.3	28.6	64.3
10,001 –	30,000	20,001 –	55,000	20	50.0	75.0	90.0
>	30,000	>	55,000	70	85.5	97.9	100.0

CD4+ cell count 200–350[**] and HIV levels[†] of …

bDNA		RT-PCR		Percent of AIDS-defining illness[‡]			
				n	3 years	6 years	9 years
≤	500	≤	1,500	3[§]	—	—	—
501 –	3,000	1,501 –	7,000	27	0.0	20.0	32.2
3,001 –	10,000	7,001 –	20,000	44	6.9	44.4	66.2
10,001 –	30,000	20,001 –	55,000	53	36.4	72.2	84.5
>	30,000	>	55,000	104	64.4	89.3	92.9

CD4+ cell count > 350 and HIV levels[†] of …

bDNA		RT-PCR		Percent of AIDS-defining illness[‡]			
				n	3 years	6 years	9 years
≤	500	≤	1,500	119	1.7	5.5	12.7
501 –	3,000	1,501 –	7,000	227	2.2	16.4	30.0
3,001 –	10,000	7,001 –	20,000	342	6.8	30.1	53.5
10,001 –	30,000	20,001 –	55,000	323	14.8	51.2	73.5
>	30,000	>	55,000	262	39.6	71.8	85.0

FOOTNOTES FOR MELLORS' CHART

[*]   Data from the Multi-Center AIDS Cohort Study (MACS) (Source: JMellors JW, Rinaldo CR Jr, Gupta P, et. al. Prognosis in HIV-1 infection predicted by the quantity of virus in plasma, *Science* 1996; adapted by Alvaro Muñoz, PhD, John Hopkins University, 2001)

[†]   MACS numbers reflect viral load values obtained by 2.0 bDNA testing. RT-PCR values are consistently 2–2.5 fold higher than bDNA values, as indicated.

[‡]   In the reference study, AIDS was defined according to the 1987 CDC definition, which did not include asymptomatic persons with CD4+ cells <200.

[§]   Too few subjects were in the category to provide a reliable estimate of AIDS risk.

[**] A recent evaluation of data from the MACS cohort of 231 persons with CD4+ cell counts >200 and <350 cells demonstrated that of 40 (17%) persons with HIV levels below 10,000, none progressed to AIDS by 3 years (Source: Phair JP, Mellors JW, Detels R, Margolick JB, Muñoz A. Virologic and immunologic values allowing safe deferral of antiretroviral therapy. *AIDS* 2002; 16(18): 2455-9).). Of 28 persons (29%) with HIV levels of 10,000–20,000, 4% and 11% progressed to AIDS at 2 and 3 years, respectively. Viral load was calculated as RT-PCR values from measured bDNA values.

ANTI-HIV STRATEGIES · APRIL 2008 · PROJECT INFORM

12

TOLL-FREE NATIONAL HIV/AIDS TREATMENT HOTLINE   1-800-822-7422   LOCAL AND INTERNATIONAL   415-558-9051   MONDAY–FRIDAY 10-4   PACIFIC TIME