Switching HIV Treatment

Let’s face it. No one drug—or combination of drugs—is going to work for everyone, or work forever. Studies have pretty much confirmed that for every two people who are able to stay on one regimen for a long period of time, one other is unable to keep their viral load down, CD4 cells up, or tolerate the side effects while on their first regimen.

The good news is that treatment options have greatly expanded in recent years, which helps people keep their CD4 counts as high as possible and keep HIV levels as low as possible over time. With better understanding of drug resistance and its testing—along with newer drugs specifically designed to treat drug-resistant virus—maintaining control of HIV for long periods of time is entirely possible.

Most of this article deals with switching HIV treatment due to treatment failure. However, there are other reasons for switching meds when viral load is well controlled, which is discussed directly below.

Can I switch medications when my viral load is undetectable?

Yes. Whether you’ve just started treatment or have been on it for several months or years, the following are possible reasons for switching when viral load is well suppressed.

- Reduce the number of pills, doses or drugs that are taken daily. Single tablet regimens (STR) are taken as one pill once a day and may be an option for people who take two or more meds or doses of meds daily. People who have older medications in their regimen may be able to switch to newer meds or combo pills to reduce pill count, even if it’s not an STR. Finally, “maintenance treatment” began in 2017 with the FDA approval of a medication called Juluca, which just contains two HIV drugs, may be available in certain situations.

- Improve side effects issues in the short- and long-term. If a particular side effect is negatively
affecting your quality of life, it’s possible to switch to medications that are less likely to cause that side effect. This includes short-term side effects such as a troubling rash, difficulty sleeping or persistent diarrhea, as well as long-term side effects such as an increasing level of fats (triglycerides and cholesterol) or sugar (glucose) in the blood or signs of liver damage, kidney damage or bone loss.

- Ease possible drug-drug interactions. People living with HIV also often have other chronic infections such as hepatitis B or C or develop conditions as they age such as hypertension or diabetes that also need treatment. This situation requires careful monitoring of drug-drug interactions, especially as a person medically needs more non-HIV medications. Certain HIV meds may be more appropriate depending upon the other medications a person takes.

- Ease swallowing, food or fluid needs. Trying to swallow larger pills can be a problem for some. Also, taking medications on an empty stomach or even with food may cause nausea or vomiting. There may be options to switch to in order to help ease these issues.

- Support the best use of meds during pregnancy. Some HIV medications have been better studied than others for use during pregnancy. Pregnancy can also alter the blood levels of certain HIV meds. Therefore, careful planning of an appropriate HIV regimen should be done before conception takes place and throughout pregnancy to protect the health of both the mother and child and to reduce transmission risk.

- Lower health care costs. As health care costs continue to rise in the U.S., some HIV meds cost less, including their generic versions. This could be an issue for some people as they change health insurance plans that tier high-cost HIV medicines on their formularies or see providers in health systems that use lower-cost meds. What’s key is to ensure that switching does not compromise a person’s undetectable viral load or increase side effects.

What does treatment failure mean?
Simply put, treatment failure means that one or more of the HIV medications you are taking are no
longer doing what they should. More specifically, it means that the virus has changed enough at its genetic level that some or all of the regimen no longer keeps it under control. This eventually results in a return of detectable HIV.

The best way to see if your meds are working is to directly measure the amount of HIV in the blood with viral load tests. There are two times when this is important: 1) when you first start or switch treatment, and 2) while you’re on treatment. One key point to remember is that HIV continues to reproduce even while on treatment, but at extremely low levels.

We use two terms when describing viral load. In the U.S., “undetectable” generally means that the number of copies of HIV are below 50 in a small drop of blood. Conversely, “detectable” simply means copies that are above 50, and the higher that number gets the more concerning it can be especially at high levels over time. In regular HIV care, the number 50 is what many viral load tests can count down to but no further, although other tests can go as low as 40 or even 20.

If your viral load does not decrease significantly while on treatment—or stay down while taking the drugs—you are at risk of possible disease progression. Getting routine blood work done that includes your viral load and CD4 cell count can help you determine how healthy your immune system is, how active HIV is, and when you should switch therapy.

How do I know if my treatment is not working?

If any of the following occur, it might be possible that your drugs aren’t working correctly:

- If your viral load is not below 400 after 24 weeks of starting therapy. An early way to tell if a regimen is effective is to look for a 90% drop in viral load two to eight weeks after starting therapy. For example, if your viral load is 50,000 before starting and drops to 5,000 by eight weeks, chances are good that your viral load will be less than 400 by six months. Most people should be able to achieve this if resistant virus is not present.
- If your viral load is not below 50 after 48 weeks of starting therapy. It’s reasonable to expect today’s medications to get viral load to an undetectable level well before 48 weeks. However, some people may take up to a year to get there provided that there’s a steady reduction of viral load over time.
- If an undetectable viral load becomes detectable again. It’s important to consider trends over time rather than a specific result. A detectable viral load may be a sign of treatment failure but it could also simply be a lab error or a temporary “blip.” If the blip is less than 400 copies and
only occurs once, this is somewhat common and not usually anything to worry about. If a second test confirms the first (such as virus being over 400 copies and especially if it's rising), it might be time to alter your regimen.

- If your CD4 cell count does not increase while on treatment, regardless of viral load. It certainly is not only about viral load. A CD4 count should improve, on average, by 50-150 cells during the first year on treatment. However, if you started with a low CD4 count or if you’re older, it could take more than a year to improve by this much. Changing your regimen is an option if your CD4 count does not improve by at least 25-50 during the first year. And if your CD4 count falls while on treatment, changing your medications will likely be necessary.

What causes HIV to stop responding to therapy?

- Weak drug combinations (low potency). Certain HIV drugs or combinations of drugs should only be used in a starting regimen for people with viral loads below 100,000. Conversely, certain other HIV drugs are able to reduce much higher viral loads (above 500,000) more effectively. This includes integrase inhibitors and the NNRTI efavirenz. Be sure to talk with your provider about the HIV drugs you are taking to make sure you are on a potent (strong) regimen.

- Poor absorption. Absorption refers to the amount of drug that is absorbed into the bloodstream after it is swallowed. If someone vomits often from taking HIV medications, this might affect the amount of drug that stays in the stomach and gets absorbed by the body. Some meds can be taken with or without food, but others must be taken on an empty or full stomach to ensure that they’re being absorbed. Additionally, taking antacids near the time of taking your HIV meds can affect also absorption. Make sure you understand how to take your meds with respect to food, liquids and other medicines especially antacids. Be sure to tell your provider about any nausea, vomiting or diarrhea you experience.

- Drug-drug interactions. Many drugs used to treat HIV—including all protease inhibitors and non-
nucleoside reverse transcriptase inhibitors—are broken down in the body (metabolized) by an important liver enzyme called P450. This enzyme also metabolizes other common medications, including painkillers, antifungal drugs, birth control pills and antibiotics. Because of this, P450 can either increase or decrease the amount of HIV drugs in the blood. Make sure you tell your provider about all the medications you are taking—prescription, over-the-counter and even street drugs—before starting treatment, and from then on.

- Poor adherence. Adherence refers to how well you follow your provider’s instructions about the medications you take. If you do not take your HIV meds exactly as prescribed—such as the correct number of times each day, every day—this can affect the amount of drugs in your blood and, in turn, allow the virus to flourish. If you miss doses of your meds or do not understand how to take them, discuss this with your provider or pharmacist as soon as possible.

- Drug resistance. Drug resistance—loosely defined as a series of changes, or mutations, in HIV’s genes that can make it less responsive to HIV drugs—is one of the most common and serious reasons for treatment failure. People can get infected with HIV that’s already resistant so it’s important to choose the right meds to control the virus. As well, some of the factors that can lead to drug resistance while on treatment include the factors listed above. So it’s important to understand what resistance is, how it can be avoided, and what to do if it occurs.

What if my virus becomes resistant to the medication?

We’ve come a long way in terms of managing resistant HIV. Today, decades of research help guide clinicians how to safely address the presence of resistance. Resistance tests are widely available, so providers are better equipped to deal with switching one or two drugs or an entire regimen.

When a regimen is unable to keep viral load undetectable it is usually because HIV has become somewhat or fully resistant to one or two drugs but not the whole regimen. Depending upon the type of resistance that’s present, sometimes other drugs in the same class could be used. Other times, it will be necessary to switch to a different class to keep HIV under control.

What should I switch to?

It’s all based on your treatment history and the results of drug resistance testing. Here are a few
general rules, as established by the United States Department of Health and Human Services (DHHS).

- Prior treatment with low levels of virus (50 to 200 copies): Ongoing viral load within this range generally point to a low risk for new resistance to develop. However, there isn’t consensus on how to best handle this situation. Some providers would recommend staying on the same regimen and monitor more closely while others would say to switch. A single test result in this range could also simply mean a blip, as explained above. This also is an opportunity to check in with a person’s adherence and offer additional support if needed.

- Prior treatment with levels of virus of 200–1,000 copies: Viral loads within this range—especially when they’re above 500—are at higher risk for developing drug resistance. Resistance testing should be done (best done when viral load is above 500). Decisions to switch should be same when viral load is above 1,000 (see below). If a resistance test cannot be done, then switching should be done on a case-by-case basis including whether or not a new regimen will fully suppress HIV.

- Prior treatment with virus above 1,000 copies with no drug resistance: Viral loads at this level are usually due to adherence issues. Therefore, additional support should be offered to identify ways to re-establish consistent adherence on the current regimen. A viral load test should be done soon afterwards to see if it’s back to being undetectable,

- Prior treatment with virus above 1,000 copies and drug resistance: In this case, changing to another drug(s) or regimen should occur as soon as possible to prevent developing more resistance mutations. This is especially true before the viral load continues to increase and the CD4 count starts to decline. A new regimen should contain at least two and preferably three drugs that a resistance test shows are still fully active. Certain drugs, such as etravirine (Intelence), tipranavir (Aptivus) and dolutegravir (Tivicay), were developed to overcome resistance seen in other drugs of their same class.

- Extensive prior treatment with drug resistance: Given the most recently approved new drugs, it may be possible for people with extensive treatment experience to create an effective new regimen. If that is not possible, a new medication called Trogarzo (ibalizumab) was approved in
early 2018 may be an option. Additionally, although an undetectable viral load is preferred with any switch, partial suppression can still protect a person from developing opportunistic infections and other illnesses. However, the benefits of partial suppression should be weighed against the possible danger of developing new resistance mutations.

- When a person doesn’t have the option of at least two new active drugs: It is reasonable for a person to stay on a failing regimen if they have few or no other options. In fact, it may be preferable to save any other single drug to which their HIV may be sensitive until newer drugs are available so two new drugs can be added. Even on a failing regimen, a person may still maintain their CD4 count and guard against illness. However, certain drugs should be stopped to prevent cross-resistance and preserve future treatment options. When no other drugs are available, another option may be to access an experimental therapy through single-patient access of investigational new drugs (IND).

I’ve already tried most of the HIV medications, what now?

One area to consider is what other drug(s) that you have yet to use targets HIV at a different place in its life cycle. If you’ve never tried a CCR5 inhibitor, then that’s a possible new option. With the very recent approval of Trogarzo (first drug in a new class), it may be something that could be added to your regimen.

You and your provider should review your entire medical history to find any possible treatment opportunities, including getting genotypic and phenotypic resistance tests done. This review may also uncover going back on a drug that you had originally used. If necessary, your provider could consult experts in this field, such as the Clinician Consultation Center (800-933-3413).

Another option is finding a regimen made up of more than two or three classes, and sometimes five or more drugs. If each or most of those drugs are at least partially suppressive, this “salvage” regimen might still control HIV—even if it’s at low but detectable levels for a period of time. However, the main problem with taking so many drugs, aside from inconvenience, is the potential for multiple side effects and drug interactions.

What about new drugs?

A number of new drugs are being researched today, and most hold promise for people who have resistant HIV. You can read more about these on each of our drug class pages: protease inhibitors, non-nucleoside reverse transcriptase inhibitors (NNRTIs), nucleoside reverse
Experimental drugs can often be accessed through clinical studies. (See https://aidsinfo.nih.gov/clinical-trials for possible studies, or call 800-448-0440.) People may also be able to obtain access to an experimental drug in certain circumstances without getting into the clinical study through a single-patient IND (arranged on a case-by-case basis with the help of a health care provider, the pharmaceutical company and the U.S. Food and Drug Administration).

Other key things to consider around switching:

- The main principle when switching medications is to control viral load without jeopardizing future treatment options.
- Before switching, especially when resistance is an issue, a full review of the person’s medical history should be done including past toxicities and all resistance test results or assumptions about possible resistance.
- Within the first few months of a treatment switch, individuals should be monitored more closely.
- People who live with chronic hepatitis B and who want or need to switch medications should continue to take those HIV meds that also treat their hepatitis B.
- Switching to a single drug is generally not recommended. Various studies of monotherapy have shown higher rates of treatment failure and new resistance when using just one HIV drug.
- “Maintenance treatment” is now a reality. This means switching from a durably stable regimen with three or more drugs to one with just two drugs available for certain people.
- Making decisions around switching medications can be complicated. Medical staff can discuss cases with the national Clinician Consultation Center at 800-933-3413.

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