REASONS FOR HOPE

HIV/AIDS

Path to success

A few important steps can minimize the risk of failure with combination antiviral therapies

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by The Boston AIDS Writers Group

The arrival of protease inhibitors has ushered in a new era of treatment and hope for people with HIV disease, and even for those who have progressed to AIDS. While the majority of people using combinations of antivirals with a protease inhibitor are doing very well, a significant minority fails with this type of treatment. Sometimes the virus is already resistant to the medication; other times the treatment is just not powerful enough to reduce the viral load (the amount of virus in the bloodstream) to a low enough level to prevent resistance from occurring. In some cases the drugs produce intolerable side effects or are not used as directed. In fact most, but not all, cases of treatment failure can be attributed to one of these causes.

For most people the critical issue is to prevent the development of a viral strain that is resistant to the combination of drugs they are on. Resistance can develop because the virus sometimes makes imperfect copies of itself when reproducing, and some of these copies may be able to survive and reproduce despite the antiviral combination. When a resistant virus emerges, it may make enough copies that the drugs begin to fail. This article outlines steps one can take to minimize the possibility of that happening, and addresses some options for people who are unable to tolerate a given combination.

By following these essential guidelines and working closely with a doctor who has significant experience with HIV disease, you can get the most out of the current treatment technology.

The goal of antiviral therapy is to get rid of all virus in the body or at least reduce viral load as much as possible—preferably to levels that scientists cannot detect with the most sensitive viral load tests available, which measure as low as 400 or 500 copies of the virus.

The fewer virus copies that are in the bloodstream, the lower the chance that they will mutate and become resistant to the antiviral combination you are using. It is believed that the only way to be sure that no resistant strain will emerge is to prevent any virus from reproducing. Currently it is not possible to know when that happens, but getting viral load down as low as possible is the next best thing.

The fact that an undetectable viral load is not necessarily the same as no virus is just one of a number of reasons why it is as important as ever to practice safer sex.

Know what your viral load is when beginning a new combination. This is important for two reasons. First, to make sure the drug is working. You will want to check your viral load later and compare it to your starting point. Second, you need to consider if the combination you are planning to take is strong enough to get your viral load down to undetectable levels. People with very high viral loads may want to consider something more powerful than a standard triple combination of a protease inhibitor and two nucleoside analogues (nukes).

All drugs must be taken as directed by your doctor and pharmacist. Now that researchers understand how and why resistance occurs, they are insisting that skipping doses (or even taking lower doses) can lead to viral resistance and then to drug failure. For this reason it is imperative that you are prepared to make a commitment to the treatment regimen of your choice. If you falter and miss a few doses, it is probably a good idea to find a dependable alarm-type device to remind you to take your medicine each day. Also, understand that if you miss taking a dose of an antiviral, taking it late is better than skipping it completely.

Powerful antiviral combinations provide strong pressure to stop the virus from reproducing. Any let-up due to low drug levels gives the virus a chance to mutate and eventually become resistant to the therapy.

When using a protease inhibitor, timing meals around dosing is very important. Be sure to follow all label directions, including those regarding meals and side effects. Different drugs are absorbed differently by the body. Instructions around meals are given so that enough of the drug gets into the bloodstream. Taking the drugs without paying attention to meals may mean that the body is getting too low a dose, and like skipping doses, that can lead to resistance. The protease inhibitors ritonavir (Norvir) and saquinavir (Invirase) should be taken after eating fatty foods. Nelfinavir (Viracept) should be taken with food, while indinavir (Crixivan) should be taken on an empty stomach.

It is also very important to watch out for side effects and report them to your doctor. Recently high blood sugar levels was added to the list of possible side effects of protease inhibitors.

Do not take any drugs not prescribed to you, over the counter or recreational, without first talking to your doctor. There are many drugs that can interfere with the effectiveness of HIV antivirals.

Taking antivirals with other drugs can affect the level of medicine in your body. Therefore taking the wrong types of drugs with your treatment regimen can lead to drug failure or to dangerous side effects. For this reason you need to be open with your doctor about the other drugs you might be taking. Your pharmacist can be especially helpful in this area.

Store your medications properly, especially protease inhibitors. Indinavir must always be stored in its original specially coated bottle or the drug will quickly decay. The capsule formulation of ritonavir must be refrigerated at all times or it also will decay. When calling in your ritonavir prescription to the drugstore, it can't hurt to remind your pharmacist to continue to refrigerate it until you pick it up. Improper storage can affect the strength of the drug and lead to drug failure.

Protease inhibitors should generally be used with at least two other antivirals. Each drug used sets up a different roadblock for the virus to get around if it is to successfully reproduce. Using more antivirals makes it less likely that the virus will mutate to a form that can get past all the roadblocks. Furthermore, the fewer virus copies that reproduce, the less likely it is for them to mutate and become resistant to your antiviral combination.

Do not add an antiviral to an existing drug regimen that is failing or may have already lost some of its benefit. Although this is true of any antiviral, it is especially important in regard to protease inhibitors.

If you add a protease inhibitor to a combination that isn't working at its full potential, it is similar to using the protease inhibitor all by itself. This makes it much easier for the virus to become resistant, and makes that drug useless to you in the future. When beginning a combination that includes a protease inhibitor, it is best to start out with antivirals that you've never used before. If there are no antivirals (nukes) that you have not used before, consider using a double protease inhibitor combination like ritonavir and saquinavir or a combination including both a protease inhibitor and a non-nucleoside reverse transcriptase inhibitor (non-nuke).

The use and dosages of experimental combinations of drugs should be carefully considered by both you and your doctor. This is especially true of combinations including protease inhibitors and non-nucleoside reverse transcriptase inhibitors, for example nevirapine (Viramune) or delavirdine (Rescriptor).

Experimental therapies are just that, experimental, and as such involve risks. While some new combinations (including the ones mentioned above) show great promise, they may also involve serious pitfalls such as an increase in side effects and unforeseen changes in the effectiveness of the drugs. For people who have failed a standard triple combination, or who have already used up most of the nukes now available, these combinations may be the answer, but it is important that your doctor understand and explain how these drugs interact with each other.

Don't panic if you make a mistake. While it is important not to miss many doses of your medication, it is unlikely (though not impossible) that one missed dose will lead to drug failure. Don't let one mistake unnerve you to the point that you make more mistakes, or stop the therapy. If you find that you are often missing doses, or that you avoid taking one or two of the drugs in your combination, you should consult with your doctor about whether or not you should continue to use this combination given the increased possibility of the drugs failing.

There may be bumps in the road. Of course, these guidelines are for people who are regularly taking a combination. For others there may be a more basic problem: that they cannot tolerate a drug because of its side effects. This is not to be taken lightly; some side effects can be very serious, and some (such as vomiting or diarrhea) can prevent the drugs from working effectively. If you cannot tolerate the combination you are on, consider the following:

Bad side effects may be temporary. For example, many people who take ritonavir report that after one month or so, many of their bad symptoms get better or go away.

You can change the drug causing the problem to another drug of a similar type. Many people have used this route successfully, and there are not any obvious dangers in switching as long as an extremely low viral load is maintained. However, it is possible that some method of reducing the impact of side effects is wiser than trying to change therapies. Additional drugs, including some over-the-counter drugs can alleviate side effects, and changes in diet have reportedly helped many people deal with nausea. Just because you can't tolerate a given combination doesn't mean you can't find one that you can tolerate.

Finally, if two viral load tests in a row show that your combination is failing, if at all possible you should consider changing to a new regime. As more drugs become available this will be an option for increasing numbers of people, and it is truly the best way to ensure that your therapy will work for you.

The Boston AIDS Writers Group consists of Robert Folan and Lou Pesce of ACT UP Boston; and David Scondras, Robert Krebs, Derek Libby and Larry Bresslour from Search for a Cure. For more information, write Search for a Cure, 58 Burbank St., Boston, MA 02115; call (617) 536-2474; or e-mail hope@sfac.org.