# Crack the Combination

August 1, 2000 By Maia Szalavitz

Q: I've been positive for three years. My CD4 count is at 400 and falling, so I've decided to start antiretroviral treatment. Which drug regimen is best?

Once you're sure you need the medication, my first consideration is what you can tolerate and whether you will stick to it, since adherence is key to effectiveness. I don't think any class of drugs has a demonstrated superiority. But my personal preference is to start with one non-nuke (such as efavirenz [Sustiva] or nevirapine [Viramune]) and two nukes. This regimen is better tolerated and has easier dosing than those with protease inhibitors (PIs). It's not about withholding PIs for some kind of magic later. We're actually finding that people with high viral loads don't necessarily do better with PIs than with non-nukes.

Howard Grossman, MD
AIDS specialist, New York City

The conventional wisdom has recently shifted to starting with a combo of non-nukes and nukes rather than PIs. Non-nukes are easier to take—fewer pills—whereas PI-based regimens can be complex (some require changing eating times) and have various toxicities. But our experience is longer with PI-based cocktails: We know they work well and that it's harder for the virus to develop resistance to the PIs than to the non-nukes. The non-nukes are potent, but if they fail, they fail big-time. I don't think you can say one approach is clearly better; clinical trials are under way to look at this. The important decision-making factors should include: How high is the viral load? Higher levels might suggest a PI-based combo. Are there social or psychological issues affecting adherence? Lack of stable housing and conditions such as depression can make it tough to stick to a regimen. Are there toxicities that you're particularly anxious about? Some people don't mind the low-grade, chronic diarrhea that can come with PIs. Some people worry about the agitation, insomnia and nightmares you can get with Sustiva; former drug users, for example, might have particular problems with this.

Paul Volberding, MD
Director, Positive Health Project, San Francisco

I don't recommend anything until the patient is ready. The key piece is deciding which combination you can live with over the long term. If you're worried about adherence to a complex

regimen, I would either wait until you can fully commit or consider starting with two drugs: ddI and hydroxyurea. For some people, less is more. With this regimen, pill burden and toxicity are lower, and I find that it’s well tolerated and potent. Plus it maximizes second choices. The patients I have on it have done well—most now have viral loads under 1,000—even though the viral load comes down slower. But I’d only use this combo for people with 400 or more CD4 cells. Interestingly, a recent analysis of studies of triple-combination therapy found that the fewer total pills taken, the greater the viral suppression—regardless of which drugs were used. I also recommend using a multivitamin and a broad array of antioxidants to help protect against the potential toxicity of the drugs.

Richard Elion, MD
AIDS specialist, Washington, DC

*This column contains general medical info only. Consult your physician before making treatment decisions. For more info on the government guidelines for combo therapy, click on www.hivatis.org*

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