Sean’s Trough Luck

A new test of drug levels in the blood is a must-have to make the most of your regimen. Irish eyes have smiled on Sean’s results. What about yours?

This month, Steven Miles, MD, associate professor of medicine at UCLA and director of the CARE Clinic at the university’s AIDS Institute, reviews POZ Founder Sean Strub’s protease drug-level test results and explains why too much or too little DIB (drug in blood) can cause treatment failure.

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Other than brief upward blips immediately after his two drug holidays, Sean’s viral load has remained undetectable with his combo of indinavir (Crixivan), d4T (Zerit) and delavirdine (Rescriptor). Wanting to keep it that way led his doctors to do a protease drug-level measurement (costs $60 to $80, usually reimbursed). The way that doctors understand how much of a protease inhibitor, or PI, actually stays in the bloodstream is by measuring the lowest concentration that the drug drops to just before the next dose -- the trough level. Drug levels are at their highest soon after each dose, then gradually decline. We measured Sean’s trough level for Crixivan.

We don’t do drug-level tests for nukes, like d4T, since they’re activated after they get inside the cells, making blood measurements pointless. And non-nukes are used at such high levels that they’re extremely effective, but the amounts used are unlikely to be toxic, so there’s rarely a reason to measure them.

Unlike nukes and non-nukes, protease inhibitors (PIs) are generally poorly absorbed. People’s ability to absorb and metabolize them also varies greatly. There may be only a small difference between an effective protease level and a toxic one, so taking the same dose, people can end up with very different blood levels. Low PI trough levels are associated with premature drug failure since at those low drug points the virus is not being sufficiently suppressed. Conversely, high trough concentrations cause needless toxicity. You need to dose just right: enough to inhibit the virus at all times but not so much that you cause avoidable side effects. A lot of the PI problems -- like dry skin, kidney stones or hair loss -- are largely due to excessive drug levels. Dropping the dose might maintain viral suppression but eliminate such symptoms.

At my practice, all new patients and patients who change PIs get a trough level at four weeks. We alter the dose based on results, and repeat the process every four weeks until the trough level is right. Measuring trough levels -- along with genotype (resistance testing), viral load and CD4s -- is also extremely important in determining why a patient’s regimen is failing. In our experience, two-

thirds of all patients fail protease inhibitors because of too little drug rather than viral resistance.

One way to ensure absorption is to boost PIs to a higher, more effective level to suppress the virus again. Adding ritonivir (Norvir) to saquinavir (Fort-ovase), amprenavir (Agenerase) or indinavir, for example, works well as a salvage therapy. However, toxicity is still a concern with this approach.

Sean did the test correctly, taking his previous dose as scheduled and then having blood drawn just before his next dose. His trough level was just right at 0.280 micrograms/per mililiter of blood. This helps explain why he has maintained undetectable viral load with few side effects. But for many others, doing PI drug levels and customizing doses based on the results could help prevent premature drug failure and reduce med toxicity.
