Don’t Be So Sensitive

Sean’s very low viral load on the ultra test may mean little

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Laboratory analyses can help health practitioners make diagnoses and people with HIV track their health. Steven Deeks, MD, assistant clinical professor of medicine at the University of California, San Francisco and a leading researcher on antiretroviral therapy, offers a second opinion on the ultrasensitive viral load test results of POZ founder Sean O. Strub.

Although Sean’s treatment regimen—Crixivan (indinavir), d4T (Zerit) and delavirdine (Re-scriptor)—has long kept his viral load undetectable with standard tests (which measure down to 400 viral copies), an ultrasensitive test (which measures down to 25) gave a reading of 28 copies/ml. However, the accuracy of ultrasensitives at very low levels is questionable. Those 28 copies may be virus released by long-lived cells that will die quickly without infecting other cells. And retesting is critical since this might just be a false reading.

In the May issue of POZ, Paul Bellman, MD, advised Sean to consider changing or adding drugs if a second test confirms that he’s off the undetectable list. But I still consider his regimen a success. “Drug failure” is generally defined as a viral load over 400 (with PCR) or 500 (with bDNA) after 16 to 24 weeks of therapy. So Sean’s not in this category. And although research has shown that the lower the viral load goes, the longer it stays down, we don’t really know how low is low enough. Learning what, if anything, should be done for patients like Sean whose virus is detectable only with ultrasensitive tests—and research suggests this may be true for a large proportion of those who are undetectable with standard tests—requires further research.

Even significant viral loads don’t necessarily indicate drug failure. There have been physician reports that some patients on protease-based combos do better than their viral loads would predict. In particular, many whose CD4 counts initially increased maintain both those counts and clinical stability—even after viral loads rise. In a retrospective study at San Francisco General Hospital, this was the case for the vast majority of those patients who stayed on their regimens despite viral load increases. In those followed for 12 to 18 months after viral rebounds, not on-ly were CD4 counts maintained, but very few (eight out of 143) developed opportunistic infections (OIs).

Interestingly, the common bond for patients who did develop OIs was that although some had initial viral load drops, most never achieved CD4 rises. Other researchers note that even small

CD4 increases after beginning therapy are strongly tied to better clinical outcomes. So the presence or absence of this increase may help predict where a patient is headed clinically. And we might want to consider aggressive OI prophylaxis for patients who never see a CD4 jump.

Does this mean that those people in the study who did well will never progress to more advanced disease? Absolutely not. Based on all the data, it’s likely that progression will happen sooner or later—although we don’t know when. Why these patients are doing well now is another unknown. Some researchers think that when the virus mutates to resist protease inhibitors, it may become less able to destroy CD4s. Others think that even a short-term drop in viral load allows the immune system to bounce back, and that its improved function is sustained for some period after the virus resurfaces. Only additional research can clarify this.

Meantime, the central question for patients less lucky than Sean in maintaining very low or undetectable viral loads is how therapies should—or should not—be adjusted in response to significant viral load changes. As always, decisions must be individualized. Most evidence supports the idea that suppressing viral replication reduces the likelihood of drug resistance, which in turn keeps therapies working longer. So maintaining the lowest possible viral load is ideal. If the viral load is significantly increased, a patient who still has some good drug-combo choices might want to aim for undetectable by switching therapies. On the other hand, someone with no good options might consider retaining the current combo, if side effects don’t outweigh benefits.
