Could Switching HIV Therapy Early Avoid Treatment Failure?

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Switching an antiretroviral (ARV) regimen within three months of starting treatment could significantly increase the odds of treatment success and decrease the risk of developing drug resistant virus. This is the conclusion of researchers using a complex computer model, published in the March 24 issue of the online journal *PLoS One*.

As good as current ARV regimens are—and they are quite potent—anywhere from 10 to 25 percent of people who start treatment for the first time experience treatment failure within their first year. What's more, these data come from the more controlled world of a clinical trial, and experience outside of such trials indicates that failure rates are even higher in real-world settings.

The consequences of early treatment failure can be significant. Mostly notably, the development of drug resistance limits the ability to construct new, potent and tolerable regimens in the future. This is because once new mutations of HIV appear, some of them get saved inside latently infected CD4 cells (HIV-infected immune cells that "go to sleep" and thus avoid destruction from the immune system or HIV drugs). The virus inside those latent cells can come roaring back to life as soon as a person tries to restart a drug to which they'd once been resistant.

In an effort to boost early treatment success, and to avoid the archiving of resistant virus inside latent cells, Max von Kleist, PhD, from the Freie Universität in Berlin, and his colleagues ran complex computer simulations of a new strategy that involves switching treatment within days of starting a new regimen.

First von Kleist's team created "virtual" patients using data from a variety of types of clinical trials. This allowed them to establish a "baseline" for how often initial treatments fail and how quickly drug resistant viruses emerge and get archived. The researchers figured that, on average, most treatment failures begin occurring about four months after a person starts HIV treatment for the first time, and that resistant viruses begin to be archived much sooner than that.

Based on this first set of data, von Kleist and his colleagues figured that switching treatment sometime before that four-month point would not only make subsequent treatment failures less likely, but also stop the process of archiving drug resistant strains so early that the drugs from the initial regimen could be used again in the future.

After trying different strategies in thousands of virtual patients, von Kleist and his team came up with what they felt would be the ultimate strategy. This new plan involved having participants start an initial induction regimen containing a Norvir (ritonavir)–boosted protease inhibitor combined with an integrase inhibitor and an entry inhibitor. After 80 days on the induction regimen, they would then switch to a maintenance regimen containing two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse transcriptase inhibitor.

In the computer simulations, von Kleist's team found that the new strategy dropped the treatment failure rate from 18 percent over two years' time to less than 4 percent. Moreover, the number of archived drug-resistant strains of virus was many times lower, thus greatly increasing the chance that the drugs used in the induction regimen could be taken again in the future.

The authors acknowledge that computer simulations are a far cry from real-world experience. They note, however, that the results from their study are substantial enough to warrant a clinical trial in people.
