



Full viral suppression newest trend seen in the "post-HAART" era

New immunotherapy treatment could help with trend

In what might be called the post-HAART era, there is an encouraging new trend of clinicians seeing greater numbers of patients who have undetectable viral loads, according to an HIV clinician who has been in the trenches for over two decades.

"I've been taking care of HIV patients since the mid-1980s, and I've seen all of these amazing trends emerge," says **Michael S. Saag**, MD, a professor of medicine at the University of Alabama at Birmingham (UAB), and director of the UAB Center for AIDS Research in Birmingham, AL.

"There are three eras of HIV antiretroviral therapy," Saag explains. "There's the first era of minimal or no therapy; then there's the HAART era, which began in 1996, and now we're in the success era."

Within the past two years, the new generation antiretroviral (ART) drugs have resulted in astonishing increases in patients who achieve undetectable viral loads, Saag says.

"These drugs have activity even when other drugs fail, and the convergence of two or three of these agents available at the same time, and used together, has translated into this success," he adds.

Saag estimates that during the HAART era perhaps 30 percent to 40 percent of the HIV patient population achieved full viral suppression. Prior to 1996, almost no patients achieved full viral suppression of less than 50 copies.

"Now the percentage of patients who achieve full viral suppression is between 60 percent and 65 percent," Saag says.

The trend is even more remarkable when one considers that at least a fifth of HIV patients have been through multiple ART regimens, and some of these people had never obtained undetectable virus before now, he says.

"We've had a wave of better drugs that are suppressing the virus more efficiently, and patients are living longer and have a better quality of life," says **Richard B. Pollard**, MD, a professor of internal medicine and microbiology, and chief of the division of infectious diseases at the University of California, Davis Medical School, in Sacramento, CA. Pollard also is the chief medical officer of Genetic Immunity of McLean, VA, and Budapest, Hungary.

"Not all patients will respond and will take the medications, so other approaches are still indicated," Pollard adds. "If patients can tolerate the drugs, and they're taken [correctly], they can suppress the virus for a long period of time."

Still, there is room for other approaches in some patients, including an immunotherapy strategy that might prevent progression of HIV infection, Pollard says.

For instance, Genetic Immunity has been studying a medical patch, called DermaVir Patch Immune Therapy, that provides topically administered HIV immune therapy.

"We have shown in monkeys that this dermatologic patch can improve viral load and suppress infection in SIV-infected monkeys," says **Julianna Lisziewicz**, PhD, chief executive officer of Genetic Immunity.

The hope is that people who have been newly diagnosed with HIV would be given the patch for a three-hour application, every two to six months, to help reinforce their own immune response against HIV viral replication, and it could give patients more time before they would need to be placed on antiretroviral therapy regimens, Lisziewicz explains.¹

An immune approach or vaccine that slows down HIV disease progression could help decrease viral loads and provide significant public health benefits as well, Lisziewicz notes.

"I think the advantage of an immunotherapy might be that this is inducing completely normal immune response, and this is expected to have no side effects," Lisziewicz says. "So, you can really benefit from very safe treatment."

The theory is that if clinicians can stimulate HIV specific immune responses by only vaccinating at prolonged intervals, then this approach will help the patient fight HIV, says Pollard, who also is the principal investigator of the immunology specialty laboratory, chair of the ACTG Laboratory Evaluation Subcommittee and is principal investigator of the California Research Center for the Biology of HIV in Minorities, all in Sacramento.

Although the topical immune approach shows promise, it's unlikely to provide the public health prevention benefits of ARTs that achieve full viral suppression, Pollard notes.

"This therapy may prolong the time before someone needs to start antiretroviral therapy, but I don't think it will totally stop transmission of the disease so that people can't transmit HIV," Pollard adds. "This is not like a triple cocktail of ART that can suppress viral replications to undetectable levels."

It's precisely because of researchers looking outside the typical ART box and coming up with novel treatments that the post-HAART era has resulted in better tolerated and more potent HIV treatments.

The phenomenon of increasing numbers of undetectable viral loads has not been the subject of headlines or research, largely because it's so new.

Saag says his clinic has witnessed the trend and collected its own internal data regarding the increase in full viral suppression in the past two years. It began when the clinic enrolled patients in the new generation ART's expanded access programs as soon as they became available, he says.

"Most people are starting to see the same trend, but we may be ahead of the curve because we brought on all of the expanded access programs as they opened," Saag says. "So we have had access to these drugs for about a year longer than they've been on the market."

The drugs that have helped to usher in this new era include the following:

- Darunavir, a protease inhibitor that also is known as Prezista or TMC114;
- Etravirine (TMC125), a second generation non-nucleoside reverse transcriptase inhibitor (NNRTI);
- Raltegravir (MK-0518), an integrase inhibitor; and
- Maraviroc (Selzentry), a CCR5 entry inhibitor.

With previous ARTs, some patients would skip doses and take the drugs intermittently because of unpleasant side effects, Saag notes.

But the new generation of ARTs are better tolerated, which promotes adherence and helps to prevent resistance and treatment failure, he adds.

"The people who are likely to fail at this point are folks who still cannot tolerate the regimen, people with severe mental illness like depression or psychosis, or patients who have intermittent substance use of crack cocaine or methamphetamines and the like," Saag says. "They become less reliable in terms of taking medicine regularly."

What makes the new generation of drugs' potency all the more remarkable is that the Birmingham clinic's patient population includes all of the above, as well as a great number of other patients who have economic and other barriers to adherence.

"We take care of patients from all walks of life," Saag says. "Half of our new patients don't have health insurance, and those who do have insurance are sometimes underinsured."

Close to half of the patients are minorities, and 20 percent to 40 percent have had active substance use in the past, Saag says.

"In terms of economic status, our patients are a pitch lower than the general medical clinic," Saag says.

If the trend continues nationwide, there are theoretical public health benefits that might be reaped, Saag suggests.

An increase in undetectable viral loads could translate into less HIV transmission.

"There is emerging data that if you can get somebody's viral load to less than 50 copies, then they're less infectious to other people if they have an exposure," Saag says.

For example, if a pregnant woman is infected with HIV, she has a 20 percent likelihood of transmitting HIV to her offspring, he says.

"If she goes on antiretroviral therapy in the second or third trimester and gets her viral load down to below 50 copies, the likelihood of transmission is next to zero," Saag adds.

Reference:

1. Lisiewicz J, et al. Single DermaVir Patch treatment of HIV+ individuals induces long lasting, high magnitude and broad HIV-specific T cell responses. Abstract presented at the 15th Conference on Retroviruses and Opportunistic Infections, held Feb. 3-6, 2008, in Boston, MA.

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