At the End of Your Rope?

Ironically, the success of today's antiretroviral treatments has hindered the development of new options for longtime survivors with drug-resistant HIV.

September 27, 2010 By Tim Murphy

Chad Kenney, 56, was always aggressive when it came to his HIV treatment. Shortly after his 1987 diagnosis, the Denver native started a treatment newsletter, *Resolute*, that quickly became a survival guide for people living with HIV/AIDS in Colorado. He was always game to try to raise his CD4 levels with the latest drug (they've never been above the 400s), whether it was Retrovir, the first HIV med; Compound Q, a failed hope; or the very first protease inhibitor. He remembers attending a lecture in the late '80s given by the late legendary treatment activist Martin Delaney. "[Delaney] asked, 'If you had a diagnosis of cancer, would you wait and see if it got worse [before] you started to treat it?'" remembers Kenney. "So I decided that I was going to try whatever agent I could find [to fight my HIV]."

But what neither Kenney nor HIV experts knew at the time was that adding just one new drug to a failing HIV regimen is usually not enough to quash viral replication. And, doing so often leads to the rapid development of HIV resistance to one new drug after another.

An accumulation of drug-resistant mutations certainly hasn't made things easy for Kenney. Despite using a power regimen consisting of Truvada, Isentress and Selzentry, his viral load stayed in the hundreds of thousands.

It was only when he added another new drug, Prezista, that his CD4 cell count rose to 145 and his viral load fell to 69—just above the "undetectable" viral load threshold.

He's hoping these numbers will stick, if not improve. "I've lived with uncertainty for a long, long time," he says, "so I try not to ride an emotional roller coaster." But the scary truth is, if his viral load creeps back up, there's no new HIV drug on the market he can add to his regimen.

Just five years ago, tens of thousands of HIV treatment veterans were in the same boat Kenney finds himself in today. The volume of people facing treatment failure was enough to spur drug companies to develop a new wave of antiretrovirals strong and innovative enough to keep drug-resistant HIV in check. Many of those drugs on the market today—including Aptivus, Fuzeon,

Intelence, Isentress, Prezista and Selzentry—have lowered the number of people with HIV who are fully resistant to treatment. Based on most good accounts, there are just a few thousand such people nationwide.

Good news, unless you are a member of this large handful of people—which is expected to grow in size in the future—who still need new options. The number of patients who currently need resistance-busting antiretrovirals is so small that pharmaceutical drug companies have little financial incentive to invest the billions of dollars arguably necessary to develop new drugs, including entirely new classes of compounds.

“HIV drug development is about to come to a halt,” says Jay Lalezari, MD, a San Francisco HIV doc who works on creating new HIV drugs and says that of 1,000 patients in his HIV practice, only about 40 “are waiting for something better to come along.”

Nelson Vergel, a longtime HIV survivor in Houston, only recently got his viral load undetectable, thanks to TaiMed Biologics’ experimental drug ibalizumab (TMB-355). He has devoted his life to finding similarly situated patients and connecting them with the trial drugs they need to suppress their HIV.

During the past 15 years, new options continued to come along for survivors like himself. But today? “They’re in deep shit,” Vergel says. “I’m really angry.”

Why angry? For one thing, the current drugs keeping millions of people alive were tested on the very folks who currently need, or may soon need, new treatment options. “The drug industry owes them a big debt,” says Steven Deeks, MD, another San Francisco HIV doc who works on the issue of drug resistance. “We should not forget this generation of people living with HIV,” he says, adding that we need to provide them with new drugs as soon as possible.

The current pipeline, however, has only a few contenders. Two notable hopefuls: the aforementioned ibalizumab, which blocks a key protein on CD4 cells so HIV can’t bind to it, is gearing up for Phase III studies; and GlaxoSmithKline’s S/GSK-572, which is currently in Phase II studies and shows some promise for folks who’ve developed resistance to Merck’s first-generation integrase inhibitor Isentress.

In recent months, two other experimental HIV drugs—Avexa’s apricitabine and Myriad Genetics’ bevirimat—were shelved. Both were casualties of weak early test results and lack of a profit motive.

In a unique activist-doctor partnership, Vergel, Deeks and Lalezari are working with the developers of TMB-355 and S/GSK-572, as well as with the U.S. Food and Drug Administration, on a program to enable patients who really need new options to go on both drugs simultaneously, before the FDA approves them, to beef up the chance of success. They hope this program will launch by mid-2011.

Kenney, who takes a fistful of meds three times a day, says he'll only sign up for the new drug program if his current regimen doesn't hold out, but he's hoping it does. Meanwhile, life goes on. And though he and others like him may dream of "undetectable," their lab numbers don't necessarily reflect how they feel day to day.

Many patients with no options left remain in good health, living functional lives despite low CD4 counts and high viral loads. The trick, it seems, is to stay on the best HIV regimen possible rather than going off HIV meds completely. (See "Safety Nets" on page 18.) Lalezari mentions a patient who's had one CD4 cell for the past five years. "Somehow the lethality of the virus has been weakened by all the drugs he's on," he says, adding that lab CD4 counts are a weak marker of immune health because they detect only CD4s circulating in blood, not in lymph tissues and other compartments.

Kenney hopes to visit his boyfriend this winter in Thailand. For now, he hits the gym daily and eats healthy. And there's love in his life in Denver. "My brother lives two blocks away, and I have friends that go back more than 20 years," he says. And at day's end? "My 7-year-old Lab retriever, Kasandra, sleeps on my bed. She's very, very affectionate—and incredibly demanding!" Sounds a bit like her owner.

Safety Nets

Detectable virus doesn't mean doom! Here's how to survive and thrive at the end of your treatment rope while waiting for new options.

DETECTABLE? KEEP TAKING YOUR MEDS!

Research shows that people with multidrug-resistant virus and detectable viral loads do better when they stay on their "failing" HIV meds rather than going off them. Talk to your doctor about finding the best regimen possible. And it's OK to ask for a second opinion. The indefatigable Nelson Vergel can put you in touch with an expert in your area.

SUPPRESS YOUR HERPES

If you have genital herpes (HSV-2), stick to your anti-herpes meds like acyclovir or talk to your provider about taking it. Research shows these meds also help reduce HIV viral load.

USE CONDOMS

It's important to use condoms to avoid contracting sexually transmitted infections, because getting STIs can inflame your immune system and make your HIV viral load go up. You'll also want to protect your partners from drug-resistant HIV.

LIVE WELL

Eat right, exercise, take quality vitamins and reduce stress with yoga, acupuncture, support groups, a pet—whatever works for you. "Keep a positive outlook," Vergel says. He should know—he's had detectable virus most of his 27 years with HIV, and he's still going strong!

PLUG IN TO FUTURE RESEARCH

Connect with Vergel at salvagetherapies.org or e-mail him directly at nelsonvergel@yahoo.com. He’s your link to the latest resources for folks seeking new options.

Search aidsmeds.com and clinicaltrials.gov for the latest updates on experimental drugs ibalizumab, S/GSK-572 and other agents making their way into clinical trials.

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