Thousands blocked from 3TC

What could be the most promising HIV drug ever has limited distribution and is waiting for FDA approval

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by Rex Wockner

The Glaxo pharmaceutical company has stopped offering the most promising anti-HIV drug ever to tens of thousands of seriously ill people with AIDS, saying it just can't make enough to meet demand.

The drug, 3TC, which could be only months away from approval by the Food and Drug Administration, has been shown in trial studies to substantially increase CD4 immune system cells, to reduce HIV levels in blood cells by 99 percent, and to reduce levels of HIV in the bloodstream by 91 percent.

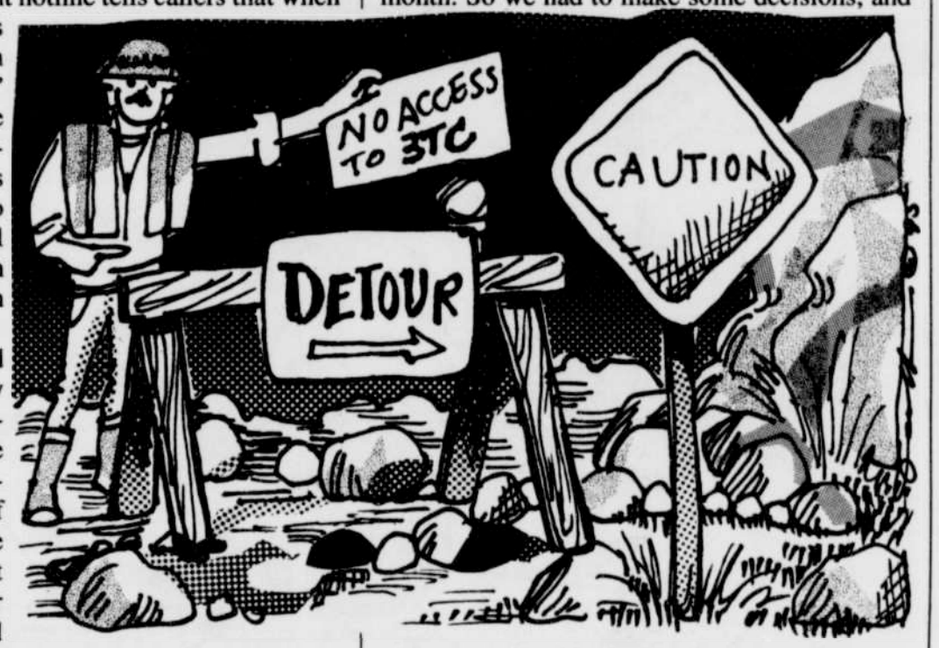
These effects, which have been shown to persist for at least one year (there have been no longer studies), occur only when 3TC is used in combination with AZT. Researchers theorize that when HIV mutates around AZT in an individual, the virus is then susceptible to 3TC, and that when it then mutates around 3TC, it mutates in a specific direction that once again makes it susceptible to AZT.

The respected *Bulletin of Experimental Treatments for AIDS* says of the 3TC/AZT combination: "[It] produces the most pronounced and prolonged effect of any anti-HIV regimen yet studied in suppressing HIV replication and increasing CD4 counts. [It is] a remarkable combination."

While awaiting completion of trial studies, Glaxo had been providing 3TC free to most people with AIDS who wanted to try the drug. But that stopped this spring, when the company announced that demand had begun to exceed supply.

Now, people with AIDS who want the drug have to prove that their CD4 cells have averaged less than 100 (approximately 1,000 is normal) on two separate tests and that they are unresponsive to or unable to tolerate the four approved anti-HIV drugs (AZT, ddI, ddC, d4T). They are then put on a waiting list—the wait is presently about 35 days. No more than 350 new patients per week are allowed to join the 24,000 already taking 3TC.

While Glaxo claims a shortage of 3TC, the Glaxo 3TC patient hotline tells callers that when the FDA approves the drug for sale in "early 1996," there will be plenty for everyone. Activists wonder if Glaxo would rather sell 3TC in 1996 than give it away in 1995.



Glaxo just paid $15 billion to buy AZT manufacturer Wellcome PLC. Glaxo's purchase of Wellcome was the second-largest business merger ever and created the world's largest pharmaceutical company, to be called Glaxo Wellcome.

"I'd like to get 3TC but I can't," says Peter Staley, founder of New York's Treatment Action Group.

"The size of the company leaves one a little skeptical," he continued. "It's the largest pharmaceutical company in the world. [But] Glaxo has been incredibly frank and open about their schedule of moving from laboratory production to factory production. Their explanation is largely that to move to larger quantities they have to do a factory shutdown of one month. When they realized they were going to have to do this shutdown, they say they made strong efforts to find a third-party manufacturer to pick up the supply shortage and nobody was able to gear up faster than Glaxo itself will be able to.

"I have my doubts about how far and wide they looked for that third party. There is some idle factory out there somewhere that could have geared up a much quicker turnaround, and Glaxo wasn't willing to pay for it," Staley says.

Glaxo's supervisor of media relations, Ramona Jones, explained the company's rationing of 3TC this way: "This is a supply issue.... We were trying to anticipate what the demand would be when we were developing supplies, and in just four months we went from enrolling about 550 patients a month to enrolling more than 4,000 a month. So we had to make some decisions, and what we realized by looking at the numbers was that we would be able to supply more patients if we paced the enrollment. Otherwise, we would have had to cut off enrollment completely with the facilities that we've got now.... We are working on the factory that makes that drug to change the equipment to handle the demand, which we were really surprised about, but the [trial study] results were surprising and encouraging."

Glaxo's 3TC media spokesperson, Jennifer McMillan, added: "When we began to build up a facility to produce 3TC, we did that without any data showing the AZT/3TC combination worked. Once we started to get data in, in late 1994, we started to figure out how many supplies we would need and we did a lot to envision the biggest Expanded Access program we could. ["Expanded Access" is an FDA classification that allows seriously ill patients to access unapproved drugs.] It was difficult to predict, but we predicted a program slightly bigger than the ddI Expanded Access program had been. We were expecting 500 or so patients a week, but during March of this year it was up to 1,000, so it was something no one in the community expected.... When we started to get those kinds of numbers, we were faced with how do we gear up. We looked at all kinds of alternatives, including contracting out manufacturing stages and utilizing other plants, and every other option we looked at was no faster than shutting down the plant this summer and upgrading it and having it come on-line this fall. [When it comes on-line], we will open up the program either by raising the CD4 count [for enrollees] or increasing the number of patients we enroll per week."

McMillan noted that Glaxo at first planned to address the shortage by simply limiting access to 3TC to 350 new patients per week but—after consultations with AIDS activists—decided to also lower the required CD4 cell count from 300 to 100 "so that the people who could least afford to wait could get 3TC sooner. The best way to do that, the activists told us, was looking at the T-cells [CD4 cells]," McMillan said.

In the meantime, as Glaxo remodels its factory, thousands of people with AIDS who have a few more than 100 CD4 cells and no longer respond to AZT, ddI, ddC or d4T, or had to stop taking them because of side effects (the most common being peripheral neuropathy, a type of serious nerve damage), are waiting for their chance to obtain the most exciting anti-HIV drug ever—waiting and, more often than not, watching their CD4 counts drop by the month.

"When I last had my blood drawn," said one person with AIDS who has 134 CD4 cells and peripheral neuropathy, "I told the nurse about the mess with 3TC access and asked her if there was some way she could make me have less than 100 T-cells. She said, 'I'll shake the vial of blood really, really hard before I send it to the lab.' "