Physician's Weekly®

December 15, 2003 Vol. XX, No. 47

In My Opinion...

HIV and AIDS: A Research and Development Update

Calvin J. Cohen, MD, MSc

Clinical Instructor; Harvard Medical School
Research Director; Community Research Initiative of New England, Harvard Vanguard Medical Associates

The HIV/AIDS epidemic began during in the early 1980s, but physicians have managed to turn what was originally viewed as a fatal disease into a chronic condition that can be controlled for life given access to life-saving antivirals. While the virus isn't going anywhere and continues to spread on a global level, optimism is still high among physicians because we continue to uncover clues from research in clinical settings. The urgency to find brand new drugs is perhaps a bit less now in the HIV community than it was in the past. The industry seems to be responding more to the critical need of the patient and is focusing on improving care with the currently available medications. Nevertheless, we have too many patients in trouble and we continue to focus on new agents to establish the health of the tens of thousands for whom current agents are just not enough.

In currently marketed products, combination tablets have been successful in treating patients with HIV and AIDS. Most clinicians have been impressed with the high success rate of a combination tablet. Some of the newer drug combination tablets can combine multiple medications to allow patients to take fewer pills from fewer bottles and there are more combination products in active development to meet this demand. This can have a positive effect on patient compliance. The general experience is that any reduction in the number of pills a patient must take during the course of a day will improve compliance and adherence. The current data suggests that at least some patients will find it easier to take their medications when they shift from taking two pills twice a day to one pill twice a day or even to just a few pills just once a day. While it's a subtle difference, it's certainly one that patients appreciate.

There are ongoing studies involving alternative approaches and combination therapies in treating patients with HIV. In the SMART study, we're comparing the effects of taking daily antiretroviral drugs to an interrupted treatment approach in which a patient takes their medication for designated periods of time, particularly when the T cells reach 250. The goal is that we want to have patients use a particular medication only as long as necessary to keep their T cell count above 250. Other studies are comparing various combinations of nucleoside analogs (NRTIs), nucleotide analogs (NtRTIs), protease inhibitors, and their effects on patients when used in various combinations.

Enfuvirtide was the first injectable fusion inhibitor to receive FDA approval and is a significant development. While no study suggests that enfuvirtide could be successfully turned into an oral pill (the drug is basically an insulin-type molecule), several drug manufacturers are trying to develop oral agent inhibitors that can work in various locations. CCR5 co-receptor blockers are the furthest along, and we are anxiously awaiting clinical assessments in the next few months.

Clinical studies suggest that all of the new classes of medications may be effective in treating patients with HIV. The physicians will need to know how to use them, and gain a sense of their toxicities as a class, but we have learned from prior experiences how to make these drugs effective for the long term. Patients can receive decades of benefits if we start them on two or three good drugs at a

time.

Physicians are hopeful that the newer HIV drugs will be far more successful than the older medications because of the learning curve that we've received from those older drugs. The industries developing the compounds are targeting resistant strains mainly because they recognize that the current drugs are actually good and that another drug is not always necessary to treat susceptible variants of HIV. At the least, the urgency is less because we now have drugs that are more powerful, easier to use, and safer.

In those who have received effective treatment for HIV, the results have been promising. When an HIV infected patient has a T cell count that increases from 50 to 250, they no longer need the infection prevention medications that they needed when the T cell count was at 50. This is very encouraging because the cellular recovery is real and not just numeric. As a result, there is less fear regarding opportunistic infections when the medications are effective. However, while there is some progress in opportunistic infection treatments, including anti-fungal medications that work against resistant strains, more treatment options are still needed.

The development of a promising vaccine for HIV has been difficult over the past 15 years because we have been unable to predict the effect of such a vaccine on patients. We're hopeful that we'll be able to predict which vaccines have a decent chance of working based on animal and in vitro data, but the question remains unanswered for now. Some animal data support that cell-mediated approaches and other types of approaches in which we generate neutralizing antibodies may be effective, and there is optimism that a vaccine could be on the way. However, proving that a vaccine is actually going to work is a huge investment of resources and a risk for vaccine manufacturers, but is certainly worthwhile.

REFERENCE LINKS:

The Centers for Disease Control and Prevention published HIV Prevention Strategic Plan Through 2005 and the complete study can be viewed online at **www.cdc.gov/nchstp/od/news/prevention.pdf**

"HIV and Its Treatment What You Should Know" is a publication of the HIV/AIDS Treatment Information Service (ATIS). The guide is available online at **http://aidsinfo.nih.gov/guidelines/adult/brochure/** ATIS provides timely, accurate information on the latest federally approved treatment guidelines for HIV and AIDS through a toll-free telephone service (1-800-HIV-0440).

The SMART trial, sponsored by the National Institutes of Health, is an ongoing study that compares two strategies for the long-term management of antiretroviral therapy for HIV and AIDS patients. The website can be found at **www.smart-trial.org**