Cancer Answers

Top oncologist Alexandra Levine breaks the great and grim news about tumors in PWAs

January 1, 2000 By Tim Horn

It's the best of times and the worst of times, according to Alexandra Levine, MD, a leading expert on HIV-related cancers. Levine, a professor of medicine at the University of Southern California (USC) and medical director of the USC/Norris Cancer Hospital in Los Angeles, confirms what many have long suspected—rates of several types of cancers are rising among PWAs, even in those HAART-takers with undetectable viral loads. But Levine is hopeful that the long, hard work of researchers will soon bear fruit. New classes of drugs in the pipeline, she argues, may revolutionize cancer care as we know it.

Tim Horn: HAART has driven down rates of opportunistic infections and deaths, but what about cancers such as Kaposi's sarcoma (KS) and lymphoma?

Alexandra Levine: There's no question that HAART has not only dramatically decreased new cases of KS, but also profoundly improved outcomes for those who have it. But with lymphoma, recent studies have found no decline. Why? Because HAART simply prolongs survival long enough to allow for the development of that cancer.

Throughout HIV disease, B-lymphocytes are constantly being stimulated in response to the virus. Since these B cells are always proliferating, there's an increased chance that an error will occur in the cellular DNA. Such errors can produce malignant [cancerous] cells such as those associated with lymphoma. Since HAART does not eradicate HIV, a low level of B-cell stimulation still occurs, even in patients with undetectable viral loads.

What other types of cancers are you seeing among people with HIV?

Anal cancer and Hodgkin's disease [a type of lymphatic cancer] are more common, and reports of testicular cancer and multiple myeloma [a type of bone-marrow cancer] are increasing. In addition, common cancers, such as lung and breast cancer, might be occurring more frequently. The challenge is figuring out how to treat these cancers in HIV positive patients, particularly those with compromised immune systems.

What is now known about the role of viruses in cancers common among PWAs?

It is safe to say that HHV-8 [human herpes virus type-8 or KSHV] is the underlying cause of KS and two other types of cancer—Castleman's disease and body cavity–based lymphoma. But HHV-8 does not act alone in causing KS tumors—immune deficiency is necessary. As for other cancers, Epstein-Barr virus (EBV) is associated with B-cell lymphomas, and human papilloma virus (HPV) with cervical and anal cancers.

Toxic chemotherapy to destroy tumor cells is now the gold standard. Do you see antiviral drugs being used in the future?

We used to treat syphilis with arsenic, but now we laugh at that. While chemotherapy has saved many lives, I hope that a few decades from now we will be able to laugh at its use for cancer—having found the way to use more targeted treatments. AIDS research will teach us to do this, as it's already taught us about the causes of some cancers.

Are any anti-HHV-8 drugs showing promise against KS?

Several drugs currently used to treat CMV [cytomegalovirus]—such as cidofovir [Vistide], foscarnet [Foscavir], and ganciclovir [Cytovene]—are active against HHV-8 in the test tube. One recent study demonstrated that patients who took either intravenous or oral ganciclovir to prevent relapses of CMV retinitis were much less likely to develop KS than those who received intraocular ganciclovir [pellets containing ganciclovir inserted into the eye] without either oral or IV versions of the drug. This was extremely exciting, as it was the first randomized, controlled study showing that treating HHV-8, although indirectly, might stop the development of KS. Several studies of these drugs are now being conducted, both for prevention and treatment of KS.

What about the drugs' side effects?

Intravenous versions of foscarnet, ganciclovir and cidofovir have been shown to cause side effects—most prominently, kidney damage or lowered blood counts—in patients taking them for CMV. If these drugs prove effective for KS, we'll likely need to use them in a similar fashion. So it will be important to think about how to make them more tolerable—and affordable.

Will these antiviral drugs be useful for lymphoma and cervical and anal cancers?

No, these drugs do not appear to be effective against EBV or HPV. Potential treatments for those viruses are still in very early stages of development.

Any other promising therapies to watch?

Yes, we're very excited about a class of drugs known as angiogenesis inhibitors. We now know that all cancers require a blood supply in order to live and proliferate. So cancer cells promote angiogenesis—the formation of new blood vessels—to promote their own reproduction. This is especially true of KS, which is a cancer of the blood-vessel walls. With angiogenesis inhibitors, we cut the blood supply to the cancer cells, ultimately halting their growth. These compounds hold a

lot of promise, not only for KS, but for all cancers.

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