# The Effect of Antiretroviral Treatment on Cancer Risk

March 8, 2011 By David Evans

People who start antiretroviral (ARV) treatments at higher CD4 cell counts are less likely to develop non-AIDS-related cancers, and treatment with protease inhibitors (PIs) might be protective against prostate cancer. These and other findings were reported in two studies presented Tuesday, March 1, and Wednesday, March 2, at the 18th Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

In the past 10 years a number of studies have documented how well combination ARV therapy diminishes the risk of developing AIDS-related cancers, and similar studies have shown recent increases in non-AIDS-related cancers—such as anal cancer. Few studies, however, have documented survival outcomes for non-AIDS cancers, and none has looked into whether PIs or non-nucleoside reverse transcriptase inhibitors (NNRTIs) have an influence on cancer as individual drug classes.

**Reasons for Concern and Hope**

To help shed light on this, Richard Novak, MD, from the University of Illinois in Chicago and his colleagues looked at a cohort of HIV-positive people enrolled in the HIV Outpatient Study (HOPS). Data were available on 7,974 people with HIV who were observed between 1996 and 2009.

Overall, the majority were younger than 40, and roughly 80 percent were male. It was a racially diverse group: About half were white, 32 percent were black, and 11 percent were Latino. The average lowest-ever CD4 count was 197, and 54 percent were current or former smokers.

During the course of the study, 241 people developed AIDS-defining cancers (ADC) and 180 developed non-AIDS-defining cancers that were due to other infectious organisms (NADCI)—such as liver cancer from hepatitis B virus (HBV) or anal cancer from human papillomavirus (HPV). Meanwhile, 220 developed non-AIDS-defining cancers that were not due to another infectious organism (NADCNI).

When all risk factors were considered, certain patterns emerged. While age at diagnosis did not influence cancer incidence, the risk for developing cancer did increase with age. In fact, for every 10-year increase in age, there was an 8 percent increase for ADC, a 15 percent increase for NADCI, and a 25 percent increase for NADCNI. Conversely, increasing CD4 counts helped protect

against cancer development. Finally, tobacco use resulted in a 300 percent increase in NADCNI.

On a positive note, Novak's team found that the five-year survival probability increased substantially over time—from roughly 60 percent in 1996 to 2000 to roughly 80 percent in 2005 to 2009.

Additionally, the higher people kept their CD4 cells the more protected they were from not only AIDS-defining cancers, but also from non-AIDS-defining cancers caused by another infection—many of which are on the rise.

"Clinicians should be aware that the elevated cancer risks among HIV-infected persons and consider screening for cancer among patients with concerning signs and symptoms as well as relevant co-infections (e.g. viral hepatitis) and behavioral risk factors (e.g. tobacco use), regardless of age," Novak's team concluded.

## Does Drug Class Influence Cancer Risk?

Michael Silverberg, PhD, from the Kaiser Permanente Northern California research branch in Oakland, California, presented data on behalf of his colleagues. He stated at the outset that their study was inspired by laboratory data indicating that PIs might have anti-tumor properties against prostate cancer. Therefore, they wondered whether either PIs or NNRTIs, and their duration, could be shown to decrease or increase certain cancer risks.

The team examined data from 12,872 HIV-positive people receiving care from either Kaiser Permanente Northern or Southern California between 1996 to 2008. During the that period there were 313 cases of Kaposi's sarcoma (KS), 159 cases of non-Hodgkin's lymphoma (NHL), 52 cases of anal caner, 42 cases of prostate cancer, 40 cases of lung cancer and 29 cases of Hodgkin's lymphoma.

Though Silverberg and his colleagues did not have complete data on the total number and types of cancer risks for each individual, they were able to capture information that was included in the database, such as age, smoking status and CD4 count.

The average age of the participants was 40 years old, 90 percent were male, and at the start of the study, the average duration of HIV infection was 2.7 years. About 44 percent had a history of tobacco use, 39 percent were overweight or obese and 22 percent had a history of drug or alcohol abuse. The average lowest-ever CD4 count was 364, and the median time spent on the two classes of ARVs was 3.6 years for PIs and 2.8 years for NNRTIs. People on either drug class were compared with people who did not take ARVs.

Taken overall, Silverberg and his colleagues did not find a statistically meaningful difference between the two drug classes, though a trend emerged for two cancers. While rates of both KS and NHL declined significantly and equally for both drug classes, there was a hint that anal cancer rates might be somewhat higher in those taking PIs. Silverberg acknowledged, when questioned

from the audience, that this difference could be due to disimilarities in how doctors screen and treat anal lesions from clinic to clinic.

There was also a hint that PIs might be more protective against prostate cancer than NNRTIs. Though the difference was small enough to have occurred by chance, the previous laboratory findings about anti-tumor activity do warrant additional analysis from other larger cohorts, Silverberg said.

"I interpret these [results] with caution," he continued. "I think these need confirmation [from other cohort studies, particularly studies where people are tracked over time]."

http://beta.docker.poz.com/article/hiv-cancer-risk-20033-3020