Cancer Burden Growing Among AIDS Patients

BY ROBERT FINN

Although AIDS-related mortality has declined since highly active antiretroviral therapy became widely available in the mid-1990s, there has been a corresponding increase in the incidence of cancer among people with AIDS, according to a study of more than 300,000 individuals.

The rates of the AIDS-defining cancers—Kaposi's sarcoma, non-Hodgkin's lymphoma, and cervical cancer—remain high in people with AIDS compared with the general population, but people with AIDS are also at high risk of several types of non–AIDS-defining cancers.

"Among those who die with AIDS and cancer, cancer now accounts for the vast majority of all deaths," said Edgar P. Simard, Ph.D., of the National Cancer Institute. "And in the entire population, non–AIDS-defining cancers represent an increasing fraction of all deaths."

Dr. Simard and his colleagues used data from 372,364 people diagnosed with AIDS in the United States between 1980 and 2006 and linked those with corresponding cancer registry records. The investigators divided their analyses into three eras: 1980-1989, when there was little in the way of effective AIDS treatment; 1990-1995, when one- and two-drug regimens were typical; and 1996-2006, when highly active antiretroviral therapy (HAART) became widely used.

VITALS

Major Finding: Among people with AIDS and non–AIDS-defining cancers, cancer-attributable mortality rose from 72% to 87% between 1980 and 2006.

Data Source: Records of 372,364 people with AIDS along with links to corresponding cancer registry records.

Disclosures: The researchers had no conflicts to report.

Since numerous studies have already been done on cancer in the 2 years following AIDS diagnosis, the investigators focused on cancer risk 3-5 years after AIDS onset, Dr. Simard said at the Conference on Retroviruses and Opportunistic Infections.

As expected, the incidence of AIDS-defining cancers was very high during years 3-5 after diagnosis. Compared with the general population, people with AIDS had 5,321 times the risk of developing Kaposi's sarcoma, 32 times the risk of developing non-Hodgkin's lymphoma, and 5.6 times the risk of developing cervical cancer, he reported.

People with AIDS also had significant increases in the risk of developing four different non–AIDS-defining cancers. They had a 27-fold increase in the risk of anal cancer, a 9.1-fold increase in the risk of Hodgkin's lymphoma, a 3.7-fold increase in the risk of liver cancer, and a 3.0-fold increase in the risk of lung cancer. Overall, people with AIDS had a statistically significant 70% increase in the risk of developing any non–AIDS-defining cancer.

The cumulative incidence of AIDS-defining cancers declined significantly. At 60 months following diagnosis, the cumulative incidence was 8.7% for the 1980-1989 era, 6.4% for 1990-1995, and 2.1% for 1996-2006, Dr. Simard said.

Yet the cumulative incidence of the four non–AIDS-defining cancers increased significantly. The 60-month cumulative incidence of lung cancer rose from 0.14% in 1980-1989 to 0.28% in 1990-1995 and to 0.37% in 1996-2006. The cumulative incidence of Hodgkin's lymphoma rose from 0.04% in 1980-1989 to 0.10% in 1990-1995 to 0.17% in the 1996-2006 era, he said.

The cancer-attributable mortality of both AIDS-defining and non–AIDS-defining cancers increased significantly from the earliest to the latest treatment eras. Among AIDS-defining cancers, the cancer-attributable mortality rose from 69% to 88%, and among non–AIDS-defining cancers, the cancer-attributable mortality rose from 72% to 87%.

Cancer prevention and treatment "will become increasingly important as survival from AIDS increases and the population continues to age," he said. ■

Lung Cancer Risk in HIV May Be Lower Than Thought

BY ROBERT FINN

The increased risk for lung cancer associated with HIV infection appears to be more modest than previous studies had indicated.

The finding is based on a study of nearly 14,000 veterans who were followed for a median of 8 years. After controlling for smoking status, age, chronic obstructive pulmonary disease, and race and ethnicity, HIV infection was associated with a 1.8-fold increase in the risk of lung cancer, Dr. Keith Sigel said at the Conference on Retroviruses and Opportunistic Infections.

Previous studies had suggested that HIV infection was associated with a 2.5-fold to 3.6-fold increase in the risk of lung cancer.

Dr. Sigel of the Mount Sinai School of Medicine, New York, and his colleagues used data from the Veterans Aging Cohort Study (VACS), a "virtual" cohort of 33,420 HIV-positive individuals and 66,840 HIV-negative controls matched by age, race, gender, and site.

The VACS data set does not include information on smoking status. In order to control for smoking status, the investigators combined the VACS data set with data from the 1999 Large Health Survey of Veteran Enrollees. The merged dataset included 3,707 HIV-infected individuals and 9,980 healthy controls.

The median age of individuals in the cohort was 48 years, and 98% were male. Minorities were well represented: 41% were white, 39% were black, 10% were Hispanic, and 10% were of other races or ethnicities.

There were some significant baseline differences between HIV-infected and uninfected individuals in the cohort. HIV-infected individuals were more likely to be current daily smokers (32% vs. 28%), were more likely to be drug abusers (16% vs. 10%), and were more likely to have lung cancer at the beginning of the study (16 vs. 38 individuals). Individuals with prevalent lung cancer were excluded from the study.

VITALS

Major Finding: HIV infection is associated with an 80% increase in the risk of incident lung cancer after controlling for smoking and other known risk factors.

Data Source: Data on 3,707 HIV-positive individuals and 5,980 HIV-negative controls.

Disclosures: The researchers said they had no disclosures.

The unadjusted absolute incidence of lung cancer was 26 cases/10,000 person-years among individuals who were HIV positive and 15 cases/10,000 person-years among individuals who were HIV negative.

Although the observed 80% increase in the risk of lung cancer associated with HIV infection was statistically significant, several other independent predictors conferred much larger risks of lung cancer. Current daily smoking was associated with a 9.8-fold increase in risk, and current occasional smoking was associated with a 3.4-fold increase in risk. Also, Hispanic ethnicity was associated with a 60% decrease in the risk of incident lung cancer.

"Our results represent a more modest risk than previous adjusted analyses, which may reflect differences in methods in our case identification, the presence of matched HIV controls for comparison within our cohort, or potentially greater precision allowed by our sample size," Dr. Sigel said. ■

HIV Drug Pipeline Diverting More Agents to First-Line Use

BY SHERRY BOSCHERT

SAN FRANCISCO — The traditional pathway to market for new anti-HIV medications is to win approval first for use in treatment-experienced patients who may have developed drug resistance, and perhaps later be considered for first-line therapy.

That may be changing.

"We now have such a robust armamentarium of regimens for our treatment-resistant patients," Dr. C. Bradley Hare said, that "our pipeline is really looking at first-line therapy, which I think is really a change in how drugs are being developed and how we analyze these drugs."

He gave three examples in the development pipeline—rilpivirine, elvitegravir, and S/GSK1349572—in a presentation at a meeting on HIV management sponsored by the University of California, San Francisco.

Follow-up data out to 96 weeks in a phase II clinical trial of 368 treatment-naive patients support 48-week data showing equivalent potency between rilpivirine and efavirenz, said Dr. Hare, medical director of the university's HIV/AIDS clinic at San Francisco General Hospital. Patients were randomized to receive 25, 75, or 150 mg/day of rilpivirine or 600 mg/day of efavirenz, along with backbone therapy consisting of two NRTI drugs.

A virologic response was seen in 71%-76% of patients, which was not significantly different between groups. Overall rates of side effects did not differ significantly.

Patients in every group developed prolongations in QTc interval, though less so with the 25-mg/day dose of rilpivirine. That dose has been selected for further study in a phase III clinical trial, Dr. Hare said.

The pattern of emergence of resistant mutations differed for rilpivirine and efavirenz. Tibotec Pharmaceuticals, which is developing rilpivirine, may coformulate the once-a-day drug with tenofovir and emtricitabine into a single, once-daily pill for triple-drug therapy, he said.

Elvitegravir, a second-generation integrase inhibitor, is being developed by Gilead Sciences. Because preliminary laboratory data look promising, elvitegravir is also being considered for development as a "quad" pill in combination with GS-9350, tenofovir, and emtricitabine, he said.

S/GSK1349572, which is being developed by GlaxoSmithKline, is another second-generation integrase inhibitor that may be headed to phase II/III clinical trials. Unpublished data from a 10-day trial of various doses or placebo in 30 patients suggested that 50 mg taken once daily reduced HIV RNA levels without need for a booster agent. ■

Disclosures: *Dr. Hare has received funding from or been a consultant, adviser, or speaker for Tibotec (which is developing rilpivirine), Gilead (which is developing elvitegravir and a rilpivirine dual formulation), GlaxoSmithKline, Roche, Merck, Bristol-Myers Squibb, Abbott, Pfizer, and Schering-Plough.*