Earlier May Be Better for Starting HIV Treatment

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MONTREAL — Mounting evidence suggests a substantial survival benefit associated with immediate initiation of antiretroviral therapy in adults with HIV, compared with deferred treatment, investigators reported at the Conference on Retroviruses and Opportunistic Infections.

Although treatment guidelines recommend starting antiretroviral therapy when CD4 T cells fall below 350 cells/mm^3 in HIV-positive adults, data from two studies presented at the conference indicate that waiting until CD4 cell counts decline to that level significantly increases morbidity and mortality, compared with starting treatment when CD4 counts are between 350 and 500 cells/mm^3.

Although starting therapy with a CD4 cell count above 350 cells/mm^3 conferred a clear benefit, no benefit was observed from starting above approximately 400 cells/mm^3.

In one of the two studies, the increased risk of death associated with treatment deferral was about 40%, according to lead investigator Dr. Mari Kitahata of the University of Washington, Seattle.

As part of the North American AIDS Cohort Collaboration on Research and Design observational study, Dr. Kitahata and colleagues compared the outcomes of 2,620 HIV-positive adults who began highly active antiretroviral therapy (HAART) when their CD4 cell counts were higher than 500 cells/mm^3 with those of 6,553 patients who deferred HAART until their CD4 cell counts dropped to 350 cells/mm^3 or below.

The relative risk of death among patients in the deferral group was 1.4, compared with the early initiators, Dr. Kitahata said.

Data from the North American and European When to Start Consortium also showed a survival advantage for earlier treatment. The findings of the retrospective examination of 15 cohort studies indicated that HIV-positive adults whose CD4 cell count was between 251 and 350 cells/mm^3 at treatment initiation had a significantly increased risk of AIDS and mortality, compared with patients who started therapy when their CD4 cell counts were between 351 and 450 cells/mm^3, according to lead investigator Jonathan Sterne, Ph.D.

All of the 21,247 patients included in the analysis began treatment for the first time when their CD4 cell count fell below 550 cells/mm^3. The investigators compared the effect of deferred and early therapy on rates of progression to AIDS or death, as well as death alone, said Dr. Sterne, of Bristol (England) University. "The adverse effect of deferring antiretroviral therapy increased with increasing CD4 threshold," he said.

Although starting therapy with a CD4 cell count above 350 cells/mm^3 conferred a clear benefit, no benefit was observed from starting above approximately 400 cells/mm^3, Dr. Sterne said. "Starting above 350, the absolute rates of mortality and absolute rates of death and dying are actually relatively low. So, the higher you put your threshold, the smaller the absolute benefit becomes," he said.

Although the findings of both studies suggest that the current treatment guidelines might be too conservative, neither study can offer a definitive answer, Dr. Sterne said at a press briefing.

Dr. Kitahata and Dr. Sterne had no financial disclosures to report. ■

Weight, Diabetes Linked to Impaired Cognition in HIV

MONTREAL — Weight control and treatment with antiretroviral drugs that are less likely to induce type 2 diabetes could reduce the risk of neurocognitive impairment associated with HIV infection, suggest study findings presented at the Conference of Retroviruses and Opportunistic Infections.

The cross-sectional observational study indicated that both waist circumference and clinical history of diabetes were strongly correlated with HIV-related neurocognitive deficits, while other components of the metabolic syndrome were not, reported Dr. Allen McCutchan, of the University of California, San Diego.

"People with HIV are living longer thanks to advances in antiretroviral therapy, but the prolonged survival is accompanied by complications of chronic HIV infection and its treatment," including the development of the metabolic syndrome and associated cardiovascular problems, Dr. McCutchan said. While the prevalence of HIV-associated dementia has diminished substantially with combination highly active antiretroviral therapy, rates of less severe asymptomatic neurocognitive impairment and mild neurocognitive disorder have risen with the aging HIV population, he said.

Dr. McCutchan and colleagues selected 145 HIV-infected individuals from a pool of 1,534 HIV-positive patients enrolled in the CNS HIV Antiretroviral Therapy Effects Research (CHARTER) study. All patients in the analysis gave a fasting blood sample. Neurocognitive impairment was determined based on a battery of neurologic assessments adjusted for age, education, and race-specific norms, and validated to detect HIV-related impairment.

Univariate and multivariate models were used to test the effects of demographics, biomarkers of HIV disease (CD4 counts, plasma HIV levels, and AIDS diagnosis), antiretroviral drug history, and metabolic syndrome–related variables on neurocognitive impairment, Dr. McCutchan explained.

The metabolic syndrome–related variables included history of type 2 diabetes, body mass index, waist circumference, blood pressure, glucose, insulin, insulin resistance, triglycerides, HDL and LDL cholesterol, and serum leptin, he noted.

Of the 145 patients included in the analysis, 53 had neurocognitive impairment, which is consistent with estimates in the literature, he said.

In univariate models, the metabolic syndrome–related variables that correlated with neurocognitive impairment included a greater waist circumference, lower LDL cholesterol levels, and an increased prevalence of type 2 diabetes.

However, "in multivariate logistic regression analysis, waist circumference, type 2 diabetes, and AIDS, but not low-density lipoprotein cholesterol or other metabolic factors, were significantly increased in individuals with neurocognitive impairment," he noted. In fact, type 2 diabetes increased the risk of neurocognitive impairment more than sevenfold, while other factors associated with metabolic syndrome, such as abnormal cholesterol or triglycerides, were not associated with increased risk.

Dr. McCutchan reported no financial disclosures related to this presentation. ■

Non–AIDS-Defining Cancer Rates Still High in HIV Patients

MONTREAL — Although the rates of AIDS-defining cancers have declined significantly among people with HIV infection since the advent of antiretroviral therapy, the rates of non–AIDS-defining cancers—particularly those associated with an underlying infectious pathogen—continue to be significantly higher than those observed in the HIV-negative population, according to data presented at the Conference on Retroviruses and Opportunistic Infections.

Michael J. Silverberg, Ph.D., of Kaiser Permanente in Oakland, Calif., presented the findings of a retrospective cohort study comparing the incidence of non–AIDS-defining cancers (cancers other than Kaposi's sarcoma, non-Hodgkin's lymphoma, and cervical cancer) in HIV-positive and HIV-negative persons during 1996-2006. With the use of data from the managed health program, Dr. Silverberg and colleagues identified 18,890 HIV-positive patients and 189,804 HIV-negative patients and followed the cohort members from first enrollment after Jan. 1, 1996.

From Kaiser Permanente cancer registries, the investigators identified incident, non–AIDS-defining cancers in the study population and grouped the cancers as infection related (anal, head and neck, liver, Hodgkin's lymphoma, and others) or infection unrelated. In the HIV-positive population, there were 482 reports of non–AIDS-defining cancers, including 220 that were infection related and 269 that were not related to infection; seven patients had both. In comparison, 3,065 non–AIDS-defining cancers were identified in the HIV-negative population, including 398 infection related and 2,698 infection unrelated (31 had both), Dr. Silverberg reported.

Calculated per 10,000 person-years, the rate of infection-related, non–AIDS-defining cancers was nearly seven times greater among the HIV-positive group, at 29.7, compared with 4.4 in the HIV-negative group, Dr. Silverberg said. Specifically, the relative risks for the periods of 1996-1999, 2000-2003, and 2004-2006, were 6.4, 7.6, and 6.2, respectively. In terms of specific infection-related cancers, the significant relative risks for anal cancer, Hodgkin's lymphoma, head and neck cancer, and gynecologic cancer were 81.4, 17.4, 2.1, and 2.9, respectively, he said.

Despite the increased risk, compared with HIV-negative individuals, "the risk of developing an infection-related non–AIDS-defining cancer did drop by approximately 4%" between 1996 and 2006, Dr. Silverberg reported. The risk of anal cancer in particular decreased in the HIV-positive population by about 6% per year, he said. During the same period, the risk of infection-related cancer remained constant among HIV-negative individuals.

The rate of infection-related, non–AIDS-defining cancers was nearly seven times greater in HIV patients.

DR. SILVERBERG

With respect to infection-unrelated non–AIDS-defining cancers, the incidence rates per 10,000 person-years were 36.4 and 30.6 for the HIV-positive and HIV-negative groups, respectively, Dr. Silverberg noted. Significant cancer-specific rate ratios were observed for kidney cancer, lung cancer, melanoma, and prostate cancer at 1.8, 1.7, 1.7, and 0.7.

The study findings may not be generalizable to women because nearly three-quarters of the cancer cases identified through the registry were men who have sex with men, Dr. Silverberg noted. He reported no conflicts of interest with respect to this presentation. ■