“This study will quantify the differences between the people who got pregnant and those who did not in terms of what they were thinking at different points in time to help assess the healthy-mother effect. This will help us relate disease outcomes to fertility outcomes, and the potential impact of patient attitudes and thought processes, and foster a deeper understanding of this complicated issue,” says Dr. Partridge.

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Human Immunodeficiency Virus Status Has No Effect on Survival in Patients With Non-Small Cell Lung Cancer

A recent study has demonstrated that human immunodeficiency virus (HIV) status in the era of highly active antiretroviral therapy (HAART) does not affect survival in patients with any stage of non-small cell lung cancer (NSCLC) (Lancet Oncol. 2012;13:1203-1209). Previous retrospective studies have suggested that patients infected with HIV had poorer outcomes than noninfected patients, but these studies included patients diagnosed before the era of HAART (J Acquir Immune Defic Syndr. 2005;39:293-299 and J Acquir Immune Defic Syndr. 2006;43:47-55). Ramesh Rengan, MD, PhD, assistant professor of radiation oncology at the University of Pennsylvania in Philadelphia, and colleagues had the goal of clarifying the role of HIV infection on prognosis in patients with NSCLC who were undergoing HAART.

Using the Surveillance, Epidemiology, and End Results (SEER)-Medicare lung cancer database, the researchers developed an analytic data set of 72,298 patients diagnosed with NSCLC from 2000 through 2005, 322 of whom were infected with HIV. There were similar percentages of patients with stage III and stage IV disease in each group, but the HIV-infected group had a significantly greater percentage of patients with stage I/stage II disease. In addition, significantly more patients in the HIV-positive group were African American (23% vs 8%; P < .0001).

The unadjusted median survival for control patients was 7 months, versus 8 months for the patients infected with HIV (P = .16). When examined based on stage of disease, the unadjusted median survival for patients with stage I/stage II disease was 37 months for controls versus 43 months for the HIV-positive group (P = .37). In the patients with stage III disease, the median survival was 7 months for control patients versus 3 months for those infected with HIV (P = .51); in the patients with stage IV disease, the median survival was 3 months in both groups. After adjustment for confounders of race, median income, sex, and comorbidities, there was still no difference in survival noted between the 2 groups.

Researchers also examined associations between HIV status and survival after definitive surgery for stage I/stage II disease. Of the 114 HIV-positive patients with stage I/stage II disease, 92 underwent definitive surgery. Among 20,016 controls, 13,640 underwent surgical resection. The median survival for the HIV-positive group was 50 months versus 58 months in the patients who were HIV negative (P = .88). The 5-year survival rate was 47% for patients who were HIV positive versus 49% in the controls (P = .88).

Clinical Implications

Given these results, the authors concluded it does not appear that NSCLC has a more aggressive nature in patients infected with HIV. Because HIV status does not appear to influence the overall survival of patients with NSCLC, a history of HIV infection should not play a role in therapeutic decision-making for patients with NSCLC. Furthermore, the authors cited a study demonstrating that 25% of trials for NSCLC specifically exclude HIV-infected patients, and concluded that this exclusion should not continue.

“This study hopefully gives strong support to the argument that HIV infection alone should not dictate therapeutic decision-making in this population,” says Dr. Rengan. “There were previous reports prior to the era of HAART that suggested lung cancer was more virulent in HIV-infected patients. Our study suggests that in the modern era of HAART therapy, that notion may no longer be true.”
One of the study’s strengths is that no patients diagnosed before the year 2000 were included, thus avoiding the improvement in stage-specific survival resulting from stage migration that was observed after the adoption of positron emission tomography scanning for staging in the late 1990s, the authors state.

Dr. Rengan notes that the main strength is that the study is to his knowledge the largest to date of clinical outcomes in HIV-infected patients with NSCLC treated in the era of HAART. “The weakness of the article is that it is retrospective and restricted to patients 65 years and older captured in SEER-Medicare. Therefore, there are issues of patient selection,” he says. “Additionally, we do not have details regarding CD4 cell count or HAART therapy in these patients (though 80% of patients do receive HAART), so granular associations between the severity of the HIV infection and outcome of the lung cancer cannot be made,” he adds.

Suresh S. Ramalingam, MD, professor of hematology and medical oncology and director of the division of medical oncology at Emory University in Atlanta, Georgia, concurs, saying, “The paper by Rengan and colleagues provides valuable information regarding survival of HIV patients with lung cancer. However, it is important to remember that a number of HIV-related factors such as CD4 count, history of opportunistic infections, and HAART therapy have an impact on tolerance of anticancer therapy and the related outcomes. The present paper does not have specific information on these issues and more importantly, included only the Medicare patient population.”

Future Directions
Survival in patients infected with HIV has increased markedly with the advent of HAART, with one study reporting a survival of 32.5 years versus 7.5 years before HAART (J Antimicrob Chemother. 2007;60:461-463). Increased survival may lead to an increased population of HIV-positive patients with NSCLC and, as noted above, patients with HIV are underrepresented in clinical trials of NSCLC treatment, with many trials using HIV status as an exclusion criterion. The authors recommend this must be changed to answer important questions in this population.

Dr. Ramalingam agrees, stating, “The majority of the ongoing studies in cancer patients exclude HIV patients on HAART therapy due to lack of data regarding drug-drug interactions. There is a clear need to study the tolerability and efficacy of commonly used anticancer agents in the HIV patient population.”

“At present, there is one prospective trial for HIV-infected patients with lung cancer that is ongoing in Europe including patients under 65 years old. I am not aware of any results from this study as of yet. I would suspect that HIV-infected patients with NSCLC under the age of 65 would fare well. Younger age has generally been shown to be associated with a better clinical outcome in lung cancer, and therefore I would expect that trend to hold in the HIV-infected population. However, this is conjecture at this point, without solid evidence,” says Dr. Rengan.

Other research questions for the HIV population relate to the elucidation of the biology of NSCLC and the available and emerging targeted therapies. “We still do not have definitive information regarding the prevalence of molecular abnormalities such as epidermal growth factor receptor (EGFR) mutation [or] EML4-anaplastic lymphoma kinase (ALK) translocation in the HIV patient population with lung cancer. It will be important to understand if there are significant biological differences between HIV-infected and non–HIV-infected lung cancer patient populations,” concludes Dr. Ramalingam.

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