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Drugs to treat anemia in cancer patients linked to thromboembolism

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Medications frequently given to cancer patients to reduce their risk of anemia are associated with an increased risk of deep vein thrombosis or pulmonary embolism, according to new research led by Dawn Hershman, M.D, M.S., co-director of the breast cancer program at the Herbert Irving Comprehensive Cancer Center at NewYork-Presbyterian Hospital/Columbia University Medical Center. The findings will be published online on Nov. 10, 2009 in the *Journal of the National Cancer Institute* (ahead of the Dec. 2, 2009 print edition).

The anemia-reducing medications, known as erythropoiesis-stimulating agents (i.e., erythropoietin and darbopoietin) or ESAs, stimulate red blood cell production and are intended to reduce the number of blood transfusions required during chemotherapy. However, concerns about the risks of deep vein thrombosis or pulmonary embolism (manifestations of venous thromboembolism) and mortality exist.

"This research answers important questions about outcomes of ESAs when used in long-term clinical practice with oncology patients," said Dr. Hershman, the Florence Irving Assistant Professor of Medicine and Epidemiology at Columbia University Medical Center, whose research is dedicated to examining cancer survivorship. "While ESAs were given to reduce the need for blood transfusions, a substantial reduction in the use of blood transfusions was not observed. However, an increase risk of deep vein thrombosis or pulmonary embolism was confirmed."

"This analysis confirms the association between ESAs and venous

thromboembolism, which was observed in previous meta-analysis," said Dr. Hershman. "This new finding is significant because where the meta-analysis looked at pooled data from randomized clinical trials, this data is from community practice - real-life clinical settings - where you can often see things that wouldn't necessarily show-up in a short-term, 12-week study. Additionally, this analysis included data from more than 50,000 patients- including those with more advanced cancer or high-risk status, who therefore might not have been candidates for clinical trials."

Based on previous findings, in the spring of 2007, the FDA required a black-box warning on ESAs about the potential for venous thromboembolism, tumor promotion, and decreased survival in ESA users. The warning suggested limiting the use of ESAs to specific tumor types, durations, doses, and targeted hemoglobin levels. In addition, the Center for Medicare and Medicaid Services proposed eliminating or limiting coverage for ESAs as treatment for some cancers.

"But what is reassuring about our findings are that they don't show an increased risk of mortality when ESAs are given with chemotherapy," said Dr. Hershman.

Dr. Hershman and colleagues analyzed the association between use of ESAs and venous thromboembolism and overall survival in patients who were 65 years or older and diagnosed with colon, non-small cell lung, or breast cancer or diffuse large B-cell lymphoma, between 1991-2002. These cancers were chosen because they were thought to be common cancers for which ESAs were frequently used. Patients were identified in the Surveillance, Epidemiology, and End Results-Medicare database, which at the time contained records of patients diagnosed with cancer in regions that represented approximately 14 percent of the U.S. population.

Results demonstrated that more patients who received an ESA developed

deep vein thrombosis or pulmonary embolism, as compared to patients who did not. Overall survival was similar in both groups. The number of patients receiving ESAs increased approximately 10-fold from 1991 through 2002, with approximately 50 percent of patients with advanced cancer undergoing chemotherapy receiving ESAs by 2002. The rate of blood transfusion per year during the same time period, however, remained constant at 22 percent.

"Further efforts at monitoring use and long-term toxicity of expensive oncology drugs should be put in place to ensure that for any drug the benefits outweigh the risks in community practice," the authors write in the paper.

In the JNCI paper, the authors note that ESAs may be of particular interest from a public policy perspective because of the costs associated with their use. Total U.S. sales of ESAs were $10 billion in 2006, accounting for a greater Medicare Part B expenditure than any other drug.

Source: Columbia University Medical Center (news : web)