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Genetic testing may be valuable in treating colorectal cancer

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For the 29,000 patients in the United States with metastatic colorectal cancer, chemotherapy with irinotecan is a standard treatment that has been shown to improve survival. But for more than one in 10 of these patients, a variation in their DNA means that this treatment could result in a severe reduction in their white blood cell count, leading to a high risk of bacterial infection and possible subsequent death. A new genetic test can identify those with the variation in order to lower the treatment dose -- however, it has been unclear whether the testing is worthwhile.

A new cost-effectiveness study led by scientists at Weill Cornell Medical College has determined that so-called pretreatment pharmacogenetic testing is only beneficial if dose-reduced treatment is shown to be nearly as effective as the full dose. If the lower dose is as effective, the test could prevent many cases of severe neutropenia, an abnormally low count of an important type of white blood cells known as neutrophils. It would also mean better life expectancy and lower cost of care.

The study appears online in the journal *Cancer* and is expected in print in the Sept. 1 issue.

"Pharmacogenetic testing is a relatively new treatment innovation that may prove to be a valuable tool for clinicians as they develop personalized treatments for cancer patients to minimize side effects while maintaining outcomes," says lead author Dr. Heather Taffet Gold, assistant professor in the Division of Health Policy in the Department of Public Health at Weill Cornell Medical College. "Our study points to

significant potential benefits for pretreatment pharmacogenetic testing for metastatic colorectal cancer, but remains to be verified by clinical research."

The study used a computer simulation model that follows hypothetical patients treated with the FOLFIRI (5-fluorouracil/leucovorin with irinotecan) chemotherapy regimen for metastatic colorectal cancer. The model assumed that under usual care, patients received a full dose of irinotecan. With genetic testing, irinotecan dosage was reduced 25 percent in individuals identified using the genetic test as having the UGT1A1*28 variant allele. The dose reduction is specified in the Food and Drug Administration-approved drug label to minimize cases of neutropenia.

Dr. Bruce Schackman, senior author of the study, says, "Cost-effectiveness evaluations of pharmacogenetic tests can provide important insights into both the clinical and economic value of these new treatment paradigms, but few of these types of studies have been conducted. Importantly, these studies also allow us to define in economic terms the value of additional comparative effectiveness research. In this case, we've determined that further research of up to $22 million should be conducted to study the risks and benefits of dose reductions based on the results of the genetic test."

Dr. Schackman is associate professor of public health and chief of the Division of Health Policy in the Department of Public Health at Weill Cornell Medical College.

"This study is an important example of how the combined use of cost-effectiveness analysis and pharmacogenetic testing can improve treatment outcomes," says Dr. Alvin I. Mushlin, Professor and Chairman of the Weill Cornell Department of Public Health. "Both methods are becoming increasingly integral to the advancement of evidence-based

medicine."

Source: New York-Presbyterian Hospital