MedicalXpress

Three 'targeted' cancer drugs raise risk of fatal side effects

February 6 2012

Treatment with three relatively new "targeted" cancer drugs has been linked to a slightly elevated chance of fatal side effects, according to a new analysis led by scientists at Dana-Farber Cancer Institute. They added that the risk remains low, but should be taken into account by physicians and patients.

The incidence of fatal complications was 1.5 percent in patients who received any of the three drugs, which block the vascular endothelial growth factor (VEGF) tyrosine kinase receptors in cancer cells, according to the study published February 6 in the Journal of Clinical Oncology. This is compared to a 0.7 percent incidence in patients given standard treatments or placebos.

The study looked at three drugs: sorafenib (Nexavar), sunitinib (Sutent), and pazopanib (Votrient). Sorafenib is approved to treat kidney and liver cancer, sunitinib to treat kidney cancer and gastrointestinal stromal tumor (GIST), and pazopanib to treat kidney cancer.

The authors of the study, led by Dana-Farber's Toni Choueiri, MD, suggest that physicians give full consideration of the potential risk before using the targeted drugs with patients at slightly high risk for bleeding or heart attacks -- the most common fatal adverse events seen in clinical trials. They also recommended that physicians and patients be aware of the risks and to consider if those patients need to be closely monitored.

"There is no doubt for the average patient, these drugs have benefits and

are FDA-approved for these indications," said Choueiri. "While the absolute incidence of these fatal side effects is very small, the relative risks are higher and patients and practitioners need to be aware of it."

For example, he said, it might be necessary to temporarily stop treating a patient with the drug or to cancel an elective surgery while a patient is taking one of these drugs. Choueiri added that these drugs should be used cautiously in patients who have had heart attacks. "The patient should be given all the information, and then he or she can balance the pros and cons in deciding whether to take the next step into treatment."

Choueiri said he believed the study is the first meta-analysis of published controlled trials to show a significantly increased risk of death from treatment with these VEGF-tyrosine kinase inhibitors. The majority of patients who died suffered fatal bleeding; the second most common cause was heart attack or heart failure; liver failure was also seen.

The 10 clinical trials subjected to the meta-analysis included 4,679 patients treated with the drugs.

Vascular endothelial growth factor receptor is a tyrosine kinase molecule that responds to chemical signals secreted by tumors to encourage the formation of new blood vessels for the purpose of providing nutrients to support tumor growth. However, humans need vascular endothelial growth factor (VEGF) at low levels to maintain critical to several physiologic processes in the body, including wound-healing, cardiac homeostasis, and formation of new blood vessels in normal tissues. As a result, blocking VEGF to treat cancer can interfere with these normal functions, increasing the odds of adverse effects.

Provided by Dana-Farber Cancer Institute