Antifolates show promise against NSCLC subtype

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Patients with non-small cell lung cancer who have mutations in the KRAS gene should respond well to the antifolate class of drugs, according to results of a recent study conducted by Quintiles comparing human lung cancer cell lines and patients.

"Our findings indicate that when patients with lung cancer have specific changes in the KRAS gene, they become very amenable to antifolate drugs," said lead researcher Sarah Bacus, Ph.D., Quintiles senior vice president and chief scientific officer of translational research and development, oncology. "This treatment stops the KRAS gene from being expressed in cancer cells and they die because they depend on this gene."

Bacus presented the study results at the AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics, held Nov. 12-16, 2011.

KRAS mutant non-small cell lung cancer (NSCLC) is an "aggressive form of cancer," Bacus said. "Until today, there have been limited treatment options available for those patients."

Bacus and colleagues treated human NSCLC cell lines (KRAS wild type, KRAS mutant nonamplified and KRAS mutant amplified) with the antifolates methotrexate or pemetrexed.

Results showed that KRAS wild-type and KRAS mutant amplified cells

were relatively resistant to antifolate treatment. In contrast, antifolates inhibited growth in KRAS mutant nonamplified cell lines. The researchers also discovered a potent downregulation of KRAS gene expression in treated cells. Bacus reported dramatic and prolonged responses to pemetrexed therapy in patients with KRAS mutant NSCLC.

Bacus recommended that oncologists order two tests: one looking for the KRAS mutation and the other to measure KRAS amplification. "Looking at the cancer mutations is not enough; you have to look at gene copies," Bacus said. "It is important before administering very expensive drugs to make sure that those mutations appear."

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