Can cancer drugs combine forces?

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Individuals with chronic myeloid leukemia (CML) are treated first with a drug known as imatinib (Gleevec), which targets the protein known to cause the cancer (BCR-ABL). If their disease returns, because BCR-ABL mutants emerge that are resistant to the effects of imatinib, individuals are treated with a drug known as dasatinib (SPRYCEL), which targets BCR-ABL in a different way.

However, patients that relapse after treatment with dasatinib, because BCR-ABL mutants emerge that are resistant to the effects of this drug, are now beginning to be seen in the clinic.

Researchers from Memorial Sloan-Kettering Cancer Center, New York, now suggest that treating patients with a combination of the drugs might decrease the chance of the cancer returning, or at the very least increase the time before a relapse occurs.

In the study, which appears online on August 16 in advance of publication in the September print issue of the *Journal of Clinical Investigation*, Charles Sawyers and colleagues show that 2 of 12 patients whose cancer had returned after treatment with dasatinib responded to retreatment with imatinib.

Analysis of the BCR-ABL proteins from these patients revealed that their BCR-ABL had only the dasatinib-resistance mutation. By contrast, the BCR-ABL proteins of the other patients had either a single mutation that rendered the protein resistant to both dasatinib and imatinib or had two mutations, one rendering the protein resistant to imatinib and one

rendering the protein resistant to dasatinib.

A third drug that can target dasatinib- and imatinib-resitant BCR-ABL is currently in clinical trials. The authors therefore suggest that rather than treating CML patients with the drugs that target BCR-ABL sequentially, they should receive all the drugs when they are first diagnosed with the disease so that the emergence of the drug-resistant forms of BCR-ABL might be prevented, or at least delayed.

Source: Journal of Clinical Investigation