AACR: tumor vulnerability varies with clonal evolution in ALL

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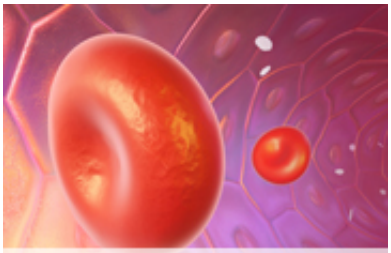

(HealthDay)—In acute lymphoblastic leukemia (ALL), tumor vulnerability to different chemotherapeutic agents varies at different stages of clonal evolution, which could represent a viable strategy in avoiding drug resistance. These findings were presented at the American Association for Cancer Research's special conference on Hematologic Malignancies: Translating Discoveries to Novel Therapies, held from Sept. 20 to 23 in Philadelphia.

Douglas A. Lauffenburger, Ph.D., from the Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology in Cambridge, and colleagues examined the efficacy of combination therapy by mathematical analysis of how tumors evolve with respect to drug sensitivity and resistance during treatment.

The researchers found that crizotinib was particularly effective in an initial pharmacological screen on murine Bcr-Abl; p19Arf−/− ALL cells, with comparable efficacy to that for imatinib. In a derivative cell line bearing spontaneous Bcr-AblT315I mutation, the efficacy of crizotinib was equivalent to that of the Bcr-AblWT parental cell line. The Bcr-AblT315I cells line showed strong resistance to imatinib, dasatinib, nilotinib, and bosutinib. Furthermore, in resistant populations derived through dose escalation treatments with dasatinib, cell populations became even more sensitive to crizotinib and foretinib.

"Rather than waiting for the tumor to become resistant to the first treatment and then thinking about a second-line drug to use, we can capitalize on opportunities that exploit vulnerabilities at different early stages, as the tumor is evolving to become resistant to the first drug," Lauffenburger said in a statement.

More information: Press Release
More Information

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