

Combination therapy targets stubborn leukemia stem cells

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New research discovers a combination of drugs that may prove to be a more effective treatment for a lethal form of leukemia. The study, published by Cell Press in the May issue of the journal *Cancer Cell*, reports that the new therapeutic strategy effectively targets notoriously intractable leukemia stem cells that often escape standard treatment and are a main factor in disease relapse.

Chronic myelogenous leukemia (CML) is a deadly form of leukemia that is associated with chromosome rearrangements that result in the expression of the BCR-ABL oncoprotein. "Treatment of CML with the BCL-ABL inhibitor imatinib mesylate (IM, Gleevec) has emerged as the first-line treatment for patients with CML," explains senior study author Dr. Ravi Bhatia, the director of Stem Cell and Leukemia Research at the City of Hope National Medical Center in Duarte, California. "However, although most CML patients initially respond well to IM treatment, there is evidence that primitive quiescent leukemia [stem cells](#) are retained in patients achieving remission after IM treatment and that these stem cells are responsible for disease recurrence."

Dr. Bhatia and colleagues were interested in examining whether histone deacetylase inhibitors (HDACi) that have shown some promise as a treatment for several other cancers, might be effective at eliminating CML stem cells. HDACi were of interest because they not only target rapidly dividing cancer cells but also have been shown to eliminate non-proliferating [cancer cells](#). The researchers found that treatment with a combination of HDACi and IM effectively reduced CML cells that were

resistant to IM alone. Further, a combination of HDACi and IM markedly diminished leukemia stem cells in a [mouse model](#) of CML.

The group went on to show that the interaction of HDACi and IM inhibited genes involved in regulating leukemia stem [cell survival](#). "Our studies indicate that treatment with HDACi combined with IM is effective against CML leukemia stem cells that resist elimination by IM alone," concludes Dr. Bhatia. "Several HDACi are in clinical development, and our studies support clinical trials of HDACi in combination with tyrosine kinase inhibitors to eliminate leukemia stem cells in patients with CML."

Provided by Cell Press

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