Temple and Fox Chase Cancer Center testing drug for cancer and bone marrow disorders

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Temple University Hospital and Fox Chase Cancer Center are the only two sites in Philadelphia that participated in an international phase I, randomized clinical trial which tested the drug guadecitabine (SGI-110) in Myelodysplastic syndromes (MDS) and acute myelogenous leukemia (AML). MDS are a group of bone marrow disorders in which the bone marrow doesn't produce enough healthy blood cells. AML is a cancer of the blood and bone marrow.

SGI-110 is a novel next generation small molecule drug which inhibits DNA methylation - one of several epigenetic mechanisms that cells use to control gene expression, the process by which genetic instructions are used to synthesize gene products. Those gene products are usually proteins and perform vital functions in the body. Aberrant DNA methylation, or abnormal methylation, has been associated with an increased rate of malignancy. SGI-110 reverses the abnormal DNA methylation.

Jean-Pierre Issa, MD, Director of the Fels Institute for Cancer Research and Molecular Biology at Temple University School of Medicine and co-Leader of the Cancer Epigenetics Program at the Fox Chase Cancer Center is lead author of the study, which has been published August 19 in the journal, *Lancet Oncology*. He says this study was the first time the drug was given to humans. "The goal was to measure the safety in patients diagnosed with MDS or AML and determine whether the drug changed the patients' epigenetic bookmarks," explained Dr. Issa.

The study revealed that SGI-110 is well-tolerated, easily administered, and biologically and clinically active in both MDS and AML patients. Importantly, potent dose-related DNA demethylation, or reversal of the abnormal DNA methylation, is associated with clinical response in patients treated with the drug, with responders showing significantly more demethylation than non-responders. "This means that the drug is safe and those patients who had more changes of their epigenome responded more to the drug," said Dr. Issa.

The clinical trial was conducted at 13 leading cancer centers in the United States and Canada, treating a total of 93 patients (74 AML and 19 MDS).

"This study has led to a large phase II study that has not yet been published" said Dr. Issa. "The most exciting outcome of these studies is that this drug also started a new phase III clinical trial, and if successful, it can lead to FDA approval to treat leukemia patients." This phase III study was just opened at Fox Chase Cancer Center by Patricia L. Kropf, MD, Assistant Director of the Temple Bone Marrow Transplant Program.

Provided by Temple University