

# SU2C partnership results in new, potent epigenetic drug for myelodysplastic syndromes, leukemia

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As a result of collaboration between academic and pharmaceutical scientists, made possible by a Stand Up To Cancer research grant, researchers may have discovered a new, potent epigenetic drug that could safely alter the way cancer cells function within the body, according to data presented at the AACR Annual Meeting 2012, held here March 31 - April 4.

The epigenetic code studied can be thought of as small tags that decorate DNA and provide instruction for how the body uses DNA, according to Jean-Pierre Issa, M.D., professor of medicine and director of the Fels Institute for Cancer and Molecular Biology at Temple University in Philadelphia, Pa. In [patients](#) with cancer, this code has become abnormal. DNA methylation inhibitors are drugs that try to normalize these tags and the code of cancer cells.

"I compare it to war and diplomacy," Issa said. Traditional cancer drugs declare war on cancer cells by killing them. In contrast, DNA methylation inhibitors use "diplomacy" and try to alter [cancer cells](#).

"These drugs try to remind the cancer cell of its normal origin and proper behavior," he said. "They remove these 'tags' and rewrite the instruction manual."

Using Stand Up To Cancer's grant model of collaborative research, Issa

and colleagues worked with Astex Pharmaceuticals to develop SGI-110, a novel DNA methylation inhibitor that is a modified form of an existing epigenetic treatment, decitabine. According to Issa, decitabine currently has limited efficacy because it is quickly degraded in the body. SGI-110 has the potential to demonstrate prolonged drug exposure and improved efficacy through protection from degradation.

Issa and colleagues conducted a phase I trial to establish a biologically effective dose and tolerability of SGI-110 in patients with either myelodysplastic syndrome or leukemia - a novel approach that differs from traditional use of the maximum tolerated-dose trial design.

In the first-in-human study, researchers randomly assigned patients with relapsed or refractory intermediate- or high-risk myelodysplastic syndrome or leukemia to subcutaneous daily injections of SGI-110 for five days or to weekly injections for three weeks.

To date, Issa and colleagues have recruited 66 patients. Results indicated that SGI-110 is well tolerated, with local injection site pain, neutropenia, thrombocytopenia and anemia as observed adverse effects.

In addition, data revealed that SGI-110 has an extended half-life and produces clinical response. At least two patients have had disease remission, with one complete response and one partial response. Issa presented complete safety and efficacy results during the meeting.

"There have been some remarkable results in patients who have no options left to them," Issa said. A phase II study will soon be under way to further explore SGI-110 doses. In addition, Issa and colleagues are beginning to design studies exploring the use of the drug in other, more common solid tumors such as lung cancer and breast [cancer](#).

Provided by American Association for Cancer Research

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