

New approach to adding study drug to chemo for melanoma treatment

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Researchers at Duke University Medical Center have just completed a clinical trial that showed it is possible to study a new combination of drugs against a melanoma recurrence that has not spread beyond a limb. Using a fairly new technique called isolated limb infusion (ILI), they tested an additional drug, called ADH-1, along with a melanoma chemotherapy drug, melphalan. They tried the ADH-1 in an effort to see if this would improve patients' antitumor responses.

“This technique showed that it is possible to use multiple drugs to treat a melanoma tumor in an isolated limb safely,” said Douglas Tyler, M.D., professor of surgery at Duke University Medical Center. “This technique may also work with other solid tumors identified in limbs.”

The advantage of isolating the affected limb during [chemotherapy](#) delivery is that doctors can give many times more chemotherapy than could be given systemwide to a patient, because only the tissues and structures of the limb are affected, as opposed to organ systems.

Although ADH-1 didn't improve the outcomes of using melphalan alone among the 45 patients, “we think this study is a good demonstration of a much less invasive way to test new compounds or combinations of drugs in certain cancer patients, while avoiding bad side effects,” Tyler said.

Isolated limb infusion is a relatively new technique, used most often in [melanoma](#) patients, in which a tourniquet is applied to a limb before the infusion of cancer-killing drugs, to keep these drugs from entering the

patient's general blood circulation. The tourniquet is applied for a limited amount of time and the patient is monitored.

“To the best of our knowledge, this phase II trial is the first prospective multicenter isolated limb infusion trial and the first to incorporate a targeted agent in an attempt to enhance the antitumor responses to regional chemotherapy,” Tyler said. He said a next step would be to try a different dosing regimen with ADH-1, because of the promise of earlier findings.

ADH-1 can cause a disruption of N-cadherin adhesion complexes that can lead to changes in intracellular signaling pathways that sensitize tumor cells to melphalan, Tyler said. “We have also showed that ADH-1 can induce changes in blood vessel permeability leading to increased melphalan [drug](#) delivery to tumors.”

More information: The study is being published in the *Journal of Clinical Oncology*.

Provided by Duke University

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