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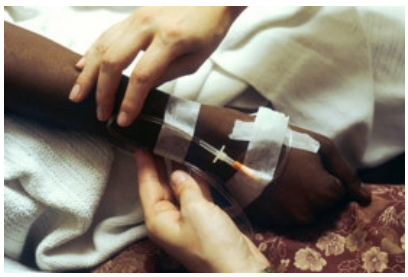
# New Drug for Stomach Cancer Starves Tumors of Blood

The medication could offer a way to fight other cancers as well

By Roni Jacobson | April 29, 2014 | 0

Last week the U.S. Food and Drug Administration approved the first treatment ever for advanced stomach cancer that has not responded to chemotherapy. The medication—called Cyramza—is from a family of drugs that were once hailed as the future of cancer treatment but have so far fallen short of expectations.



Stomach cancer is the fifth-most common malignancy in the world. There are more than 20,000 new cases in the U.S. every year, and about one million globally.
*Credit: National Cancer Institute via Wikimedia Commons*

Cyramza, owned by Eli Lilly and known generically as ramucirumab, is a type of drug known as an angiogenesis inhibitor. (Angiogenesis is the formation of new blood vessels.) Instead of targeting the tumor itself, as chemotherapy does, angiogenesis inhibitors attack the blood vessels surrounding the tumor, cutting off its supply of life-giving oxygen and nutrients. When pioneering cancer researcher Judah Folkman first showed in 1998 that tumors in mice could be starved by blocking angiogenesis, Nobel laureate James Watson infamously proclaimed, "Judah is going to cure cancer in two years."



Although angiogenesis inhibitors are not the magic bullet many doctors hoped they would be, they are still considered a promising potion for patients who have very few options. In the latest trial they extended patients' lives only modestly, but that was still a notable improvement over conventional therapy. The FDA has approved several angiogenesis inhibitors for treating cancers of the kidney and other organs, and many other clinical trials are in progress. Cyramza is the first angiogenesis inhibitor approved for stomach cancer.

Stomach cancer is the fifth-most common malignancy in the world. There are more than 20,000 new cases in the U.S. every year, and about one million globally. The incidence of stomach cancer in the U.S. has declined since the 1930s — probably due to changes in diet and food storage — the but when the disease does occur it is usually not caught until its later stages. At this point the cancer is beyond surgery or chemotherapy, and as a result, the vast majority of people with advanced stomach cancer will die within five years of their diagnosis. "There has really been a need for newer, targeted therapies that have been designed with an understanding of the basic biology of stomach cancer," says Charles Fuchs, director of the Center for Gastrointestinal Cancer at Harvard Medical School and lead investigator of the clinical trial.* "I wouldn't presume to tell you that we have achieved the proper solution to stomach cancer with this advance alone," he says, but he calls the treatment "an important first step" in developing biologically tailored drugs for stubborn cancers.

Cyramza was approved under the FDA's priority review program for medicines that show promise for treating urgent, life-threatening diseases for which other therapies are limited. The FDA also approved the drug for people with advanced tumors in the junction between the stomach and the esophagus, a type of cancer that is rising in the U.S.

Fuchs and his colleagues tested how well Cyramza worked in a randomized, controlled clinical trial of 355 patients in 29 countries. Two thirds of the people received the drug alone and the rest received a placebo. The results indicated that the compound, which is administered via an intravenous needle once every two weeks, lengthened the patients' lives by about one and a half months on average—37 percent longer than the people in the control group. Cyramza also increased the length of time that people went without

their tumors growing further, from one month to two months. Angiogenesis-inhibiting drugs stop the growth and spread of tumors, but they do not get rid of them.

Although the extended lifetimes in this trial were modest, they support the highly anticipated but elusive hypothesis that cutting off a tumor's blood supply can treat cancer, says David Cheresh, a cancer biologist at the University of California, San Diego, who was not involved in the study.

The approval comes with a "black box" warning, the strongest issued by the FDA, that Cyramza may increase the risk of hemorrhaging, potentially even fatally. The drug can also cause high blood pressure, headaches, heart attack and diarrhea.

Cyramza will become available in the next few weeks. A representative from Eli Lilly declined to specify how much it would cost. A similar antiangiogenesis drug, Avastin, mostly used to treat colon cancer, costs between $4,000 and $9,000 a month, depending on the patient's weight. Medicaid and private insurance plans typically require patients to pay about a quarter of that cost.

The high price tag coupled with relatively short increases in life expectancy have lead many health care experts to question the worth of angiogenesis-inhibiting drugs and other costly experimental therapies. Although Fuchs agrees that the overall benefit seen in this trial is modest, he points out that testing the medication in patients whose cancer has not advanced so far would likely show a better result.

In addition, most angiogenesis-inhibitor cancer medicines are not effective when taken alone, and are only approved for use in conjunction with chemotherapy. That Cyramza was found to work as a single agent is a "major advance," Cheresh says. Furthermore, in a separate trial Fuchs says that patients taking Cyramza in combination with chemotherapy experienced greater extension of their life spans.

The synergistic effect between angiogenesis inhibitors and chemotherapy may be related to a tumor's biology. Tumors hijack the chemical signal that prompts the body to form new blood vessels and use it to recruit their own blood supply. Unlike the orderly blood vessels in healthy tissue, however, tumorous blood vessels develop in a tangled web. As a result, blood flows at different rates throughout the tumor, preventing chemotherapy drugs from being distributed evenly and in some cases inhibiting their effectiveness. Researchers hypothesize that normalizing the blood flow to the malignancies with angiogenesis-inhibiting drugs may make it easier for traditional medications to penetrate and destroy the tumor. Understanding these kinds of mechanisms puts researchers closer to developing therapies tailored to the needs of individual cancer patients, Fuchs says.

"We are going to have a series of drugs that come down the pipe like that," Cheresh adds. "Their overall benefit may be marginal but their capacity to impact specific patients that we can identify upfront may be quite remarkable." In that context, he says, experimenting with drugs like Cyramza "is well worth it."

**Correction (5/1/14): This sentence was edited after posting because it incorrectly stated Charles Fuchs's position as that of lead investigator of Cyramza.*

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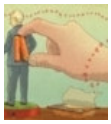


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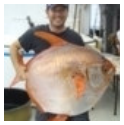

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