For advanced, HER2-amplified bile duct cancers, antibody treatment trial shows promising results

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Memorial Sloan Kettering gastrointestinal oncologist Dr. James Harding. Credit: Memorial Sloan Kettering Cancer Center

Bile duct cancers are uncommon and aggressive types of gastrointestinal

cancer. They include cholangiocarcinomas, which can form inside or outside of the liver, as well as cancers of the gallbladder, and are highly likely to cause serious disease or prove fatal.

Bile duct cancers affect the biliary tract, which consists of organs and ducts that make and store bile and release it into the small intestine. They are known as "silent" cancers, because there are usually no symptoms until they reach later stages. Surgery can be effective if bile duct cancer is caught early, but for most patients there are few good treatments.

Now, new research published June 2 in *The Lancet Oncology* and presented at the American Society of Clinical Oncology's annual meeting, finds an antibody treatment helped shrink tumors in some patients with bile duct cancers—specifically a subset of people whose tumors make a high amount of the HER2 protein, which can cause cells to multiply too quickly.

The phase 2b clinical trial, known as HERIZON-BTC-01, was a global, multicenter effort to evaluate the effectiveness and safety of zanidatamab, an antibody that works against the HER2 protein, in patients with HER2-amplifed bile duct cancer that has not responded to other treatment. Gastrointestinal oncologist James Harding, MD, of Memorial Sloan Kettering Cancer Center (MSK), and Fan Jia, Director of the Liver Cancer Institute at Fudan University in China, served on the trial's steering committee and were co-first authors of *The Lancet Oncology* study.

"Incidence of bile duct cancer has been on the rise in recent decades," Dr. Harding says. "There are currently no approved therapies targeting HER2 in these cancers, and therefore there is a significant unmet medical need. The results of this trial are very encouraging—zanidatamab shrank tumors in a subset of patients with

HER2-positive disease and was well-tolerated overall. The study illustrates the importance of molecular profiling of these cancers to allow us to match patients to precision medicines that target the features of their individual cancer."

Clinical trial results using zanidatamab against HER2-amplified bile duct cancers

The study enrolled 87 participants with HER2-amplified biliary tract cancers that were locally advanced or had spread throughout the body and for whom chemotherapy had stopped working. The patients received zanidatamab intravenously every two weeks. The antibody binds to HER2 receptors and leads to a decrease of HER2 on the surface of the cancer cells, helping to slow down their runaway growth.

The treatment was effective in shrinking tumors in 41% of the patients, the trial found. Half of patients had responses within 1.8 months, and these responses lasted 12.9 months or more in half of the patients who responded to the drug. Doctors continue to follow these patients to assess the impact of the treatment over a longer period of time.

The most common side effects of the treatment were diarrhea (37% of participants) and infusion-related reactions, such as allergic reactions, pain at the injection site, nausea, or flu-like symptoms (33% of participants). A small number of people had a decrease in heart function. No severe side effects were reported.

Zanidatamab remains under investigation and will undergo additional study to test the antibody's safety and effectiveness in a larger group of people, the researchers note. The antibody is also being evaluated in combination with first-line chemotherapies, as well as for patients with other types of HER2-expressing tumors.

The data from the trial support the potential of zanidatamab as a new targeted therapy when patients don't respond to chemotherapy, the study authors write.

"Continued research in evaluation of HER2-targeted therapies in HER2-positive biliary tract cancers is essential to improve care for these patients," Dr. Harding says. "MSK has led the development of many of these therapies over the last several decades in multiple solid tumors, and there are several ongoing studies happening in New York City and across MSK's regional sites. Moreover, we have a robust program with highly experienced surgeons in surgery for early stages of disease, and experts in radiation therapy, chemotherapy, and minimally invasive symptom relief for more advanced disease, as well as access to the latest clinical trials."

More information: *Lancet Oncology* (2023). www.thelancet.com/journals/lan … (23)00242-5/fulltext

Provided by Memorial Sloan Kettering Cancer Center

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