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UF hepatologists test chemotherapy pill in patients with advanced liver cancer, cirrhosis

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Hepatologists at the University of Florida have begun a new clinical trial in search of a better way to treat patients who have advanced, inoperable primary liver cancer but have trouble tolerating standard doses of the only drug available to help them.

Funded through a $650,000 grant from Bayer HealthCare Pharmaceuticals Inc. and Onyx Pharmaceuticals Inc., the makers and marketers of Sorafenib — the only FDA-approved drug for advanced liver cancer — the six-month, randomized pilot study will evaluate whether patients with a dual diagnosis of cirrhosis and liver cancer are better able to tolerate the drug if given doses that differ from the manufacturer's recommendation.

"The study will provide evidence for physicians about whether we can deliver more of the drug, improve tolerability and reduce adverse events by slowly introducing it," said study leader Dr. Roniel Cabrera, an assistant professor in the UF College of Medicine's division of gastroenterology, hepatology and nutrition.

UF and its Clinical and Translational Science Institute are coordinating the study, which will be carried out at 10 sites that include major Florida centers such as the University of South Florida, the University of Miami, the Florida Hospital, in collaboration with the University of Central Florida, and the Mayo Clinic in Jacksonville. The team hopes to develop a national academic consortium dedicated to advancing clinical and translational research efforts in hepatocellular carcinoma, the most

common form of primary liver cancer.

“This study is very much targeting an unmet need in oncology, and it has the potential to clarify if we actually have the right dose for the medication,” said Dr. Thom George, director of gastrointestinal oncology in the division of hematology/oncology at the UF College of Medicine, who is not directly
involved in the study. “It may help answer the question of whether more patients will derive benefit from the treatment if we just go a little slower with the dosing.”

Liver cancer, the fifth most common cancer and the third leading cause of cancer-related deaths, is a major global health problem. Despite new therapies, every year there are more than 600,000 new cases worldwide, and almost the same number of related deaths. Hepatocellular carcinoma is the leading cause of death among people who have chronic liver disease.

Many patients are diagnosed with advanced liver cancer at the same time they are diagnosed with cirrhosis, and that complicates treatment, since what works against one disease can worsen the other. When the cancer is advanced, treatment options are limited — surgery is impossible, and the most useful option left is the pill Sorafenib. It doesn’t cure cancer, but in clinical studies, patients who took it survived for three to four months longer, on average, than untreated patients.

Manufacturers recommend a dose of two 200-milligram tablets twice a day. In practice, however, those doses are too high for patients with advanced disease to tolerate. The dosing recommendation is based on clinical studies in patients whose cirrhosis was under control. But “real life” patients show up at clinics with much worse cirrhosis and have negative reactions to the drug, including severe fatigue, skin rashes, gastrointestinal bleeding and worsening of liver function. That can be

compounded by cirrhosis symptoms such as fatigue, confusion, fluid buildup in the abdomen and legs, and gastrointestinal bleeding.

“You can see how all those things can add up,” Cabrera said.

In such patients, physicians have to discontinue therapy or give less than recommended.

Cabrera and colleagues will investigate whether a “ramp up” strategy that starts with one pill a day then adds a pill a week can improve how well patients tolerate the drug, the length of time they are able to remain on it, the amount they are able to handle overall without negative effects and the effect on the cancer being treated.

“This study will take patients who are not the most healthy, and see if there is a better way to still give them every chance to increase the benefits they receive from the medication and decrease the risk,” George said. “That could potentially allow them to remain functional and be part of society and continue to work and provide for their families.”

Provided by University of Florida