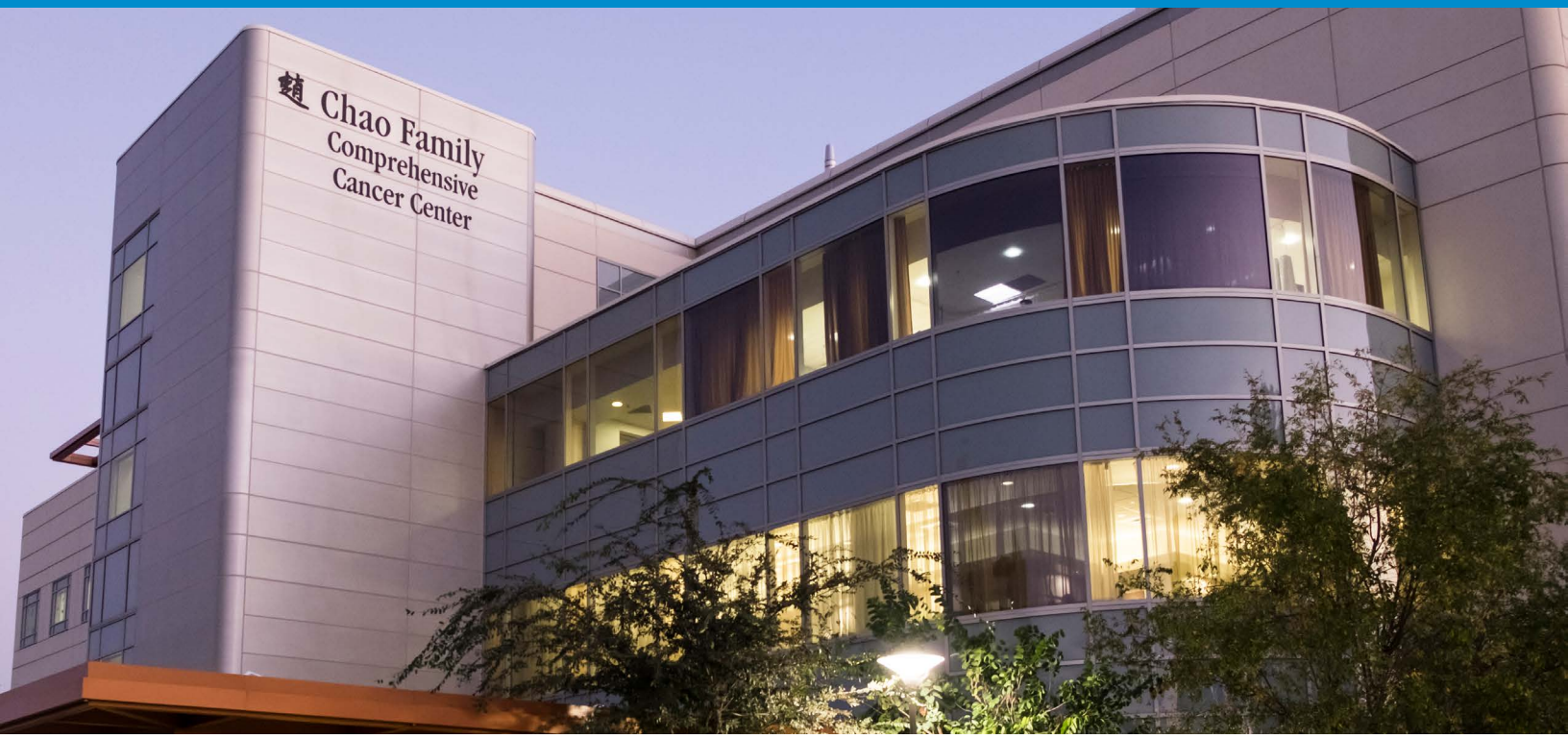

This issue of our newsletter highlights gastrointestinal cancer research and clinical trials at the Chao Family Comprehensive Cancer Center.

NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

Liver cancer trials test anti-cancer drug and tumor embolization

The UC Irvine Chao Family Comprehensive Cancer Center is recruiting hepatocellular cancer patients for two clinical trials for a treatment that proved so successful in a Phase I study that the FDA has given approval for the lead researcher to submit results for possible "breakthrough" designation.

Dr. Nadine Abi-Jaoudeh, a UCI Health interventional radiologist at the cancer center, said the results of the Phase I hepatocellular carcinoma (HCC) trial were extremely positive, with a complete response rate of 70 percent, and a 90 percent overall response, which was sustained over months. The average liver tumor size was 6 centimeters.

HCC is the fifth leading cause of cancer-related death worldwide. It is on the rise because of the increasing number of cases of Hepatitis B and C that result in cirrhosis of the liver and, ultimately, HCC.

Transarterial chemoembolization, or TACE, is the current standard treatment for HCC patients whose tumors cannot be surgically removed. TACE involves administering chemotherapy locally and embolizing, or blocking, the blood vessel nourishing the tumor. TACE extends survival but it achieves a complete response in only 15 percent to 25 percent of tumors, and an overall response rate of about 52 percent, Abi-Jaoudeh said. Recurrence within months is very common.

"It's generally seen as palliative treatment, and the outcomes have only mildly improved in 30 years," she said.

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Instead of chemotherapy in the Phase I trial, Abi-Jaoudeh and lead associate researcher, UCI Health hepatobiliary surgeon Dr. David K. Imagawa, used the experimental anti-cancer drug tirapazamine (TPZ), which becomes a free radical when a cell is hypoxic, or deprived of oxygen.

TPZ is injected by microcatheter directly into the blood vessel supplying the tumor, followed immediately by embolization. "We want it to penetrate the cells and then shut off their oxygen supply," Abi-Jaoudeh said. In the oxygen-deprived environment, TPZ attacks the cancer cells, causing necrosis and the release of antigens. The treatment, called trans-arterial tirapazamine embolization, or TATE, "was very well tolerated by patients and there were almost no side effects."

UC Irvine is the lead research site for the nationwide Phase II study that is now recruiting patients. If the Phase II trial results are similar, accelerated approval may be granted, possibly precluding the need for a Phase III trial.

Abi-Jaoudeh is seeking as many as 20 patients for the Phase II trial. They must have intermediate stage HCC tumors, with one measuring at least 4 centimeters in diameter. They also must be in good enough physical condition to care for their personal needs, such as bathing and dressing.

She also is leading a Phase IIA trial on related research for more advanced HCC cancers, adding immunotherapy to TATE. "TATE causes necrosis with antigen release into the bloodstream, which works synergistically with immunotherapy," she said. "The procedure is meant to act as a vaccine for the cancer"

The requirements for 40 patients being sought for the Phase IIA trial are essentially the same as the Phase II TATE trial, except they must have advanced stage HCC, which can include metastatic disease. However, patients cannot have received immunotherapy before consenting to the trial.

The research is sponsored by Teclison Cheery Pharma.

For more information on the research and entering the trial, contact Dr. Nadine Abi-Jaoudeh at nadine@uci.edu

Doctors with patients who may qualify for any of these trials are encouraged to contact the Chao Family Comprehensive Cancer Center's clinical research line at 877-UC-STUDY (877-827-8839) or by emailing ucstudy@uci.edu

Making a dent in colon cancer recurrence

Patients are being accepted for a colon cancer trial at the UCI Health H.H. Chao Comprehensive Digestive Disease Center to determine whether chemotherapy delivered during and within two weeks after surgery improves outcomes for patients with Stage 1 through 3 adenocarcinomas.

Currently, about 30 percent of colon cancer surgery patients experience a recurrence of the disease. "We're hoping to make a dent in that number," said UCI Health colorectal surgeon Dr. Alessio Pigazzi, the study's principal investigator and chief of the UCI School of Medicine's Division of Surgical Oncology.

Standard colorectal cancer treatment usually involves chemotherapy starting six to eight weeks after surgery, said co-investigator Dr. Mehraneh D. Jafari, assistant professor of surgery and a specialist in colon and rectal surgery. Prior studies have shown that giving chemotherapy to patients earlier is more effective, which means waiting more than six weeks significantly worsens outcomes for patients.

This Phase I clinical trial will examine whether an intravenous dose of the standard drugs (Leucovorin and 5-Flurouracil, or 5-FU) during surgery will provide a first line of attack against stray cancer cells. Once the cancer is staged, the next step in treatment will be determined. If it is Stage 1, there will be no

"This study has the potential to alter colon cancer treatment nationally by making the treatment duration shorter and more effective,"

further chemotherapy. Patients who would normally go on to receive chemotherapy based on their pathology results (for some Stage 2 and all Stage 3 cancers) would receive the next dose of chemotherapy within two weeks.

There are two possible advantages to this method, said Jafari. "The inflammatory response that occurs because of the insult of surgery potentially accelerates tumor cell growth," she said. Early use of chemotherapy treatment during surgery would address that problem.

The other issue is that patients often wait longer than six to eight weeks after surgery to begin chemotherapy. Sometimes that's because doctors are afraid chemotherapy will interfere with wound healing; often, it is delayed because patients are feeling tired for a long period of time after surgery and are unwilling to undergo more treatment.

By starting chemotherapy during surgery, she said, patients are seeing their oncologists before the operation, which helps to establish a vital the doctor-patient relationship from the outset and to better coordinate their chemotherapy treatment after surgery.

"It's a very exciting study because colon cancer is the second leading cause of cancer deaths in the United States, according to the Centers for Disease Control and Prevention," Jafari said. "This study has the potential to alter colon cancer treatment nationally by making the treatment duration shorter and more effective," Pigazzi added.

The Phase I trial underway now will include 20 to 30 patients. A Phase II trial is expected to start later this year with about 100 patients. In order to participate in in this study, patients must:

- Be at least 18 years old
- Have been diagnosed with colon cancer based on radiology studies (CT scan, MRI) or colonoscopy

Patients cannot participate if they:

- Have a certain type of colon adenocarcinoma based on results of a biopsy analysis (microsatellite instability-high tumors)
- Have been diagnosed with a metastatic disease
- Are considered at high risk when under anesthesia
- Are pregnant

The study includes three visits and takes about three to four hours for surgery and one hour for each of the follow-up visits at one week, 14 and 30 days post-surgery, over a period of 60 days.

To learn more about the trial, contact study coordinator Carlos Chavez at chavezc@uci.edu

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Making colonoscopies "smarter" with artificial intelligence

A colonoscopy may be the best test for finding colorectal cancer, but its true claim to fame is preventing colorectal cancers. The key is the detection rate of precancerous polyps called adenomas, which varies from 7 percent to 53 percent depending on the skill of the colonoscopy practitioner.

For each 1 percent increase in the adenoma detection rate (ADR), the risk of developing colorectal cancer within five years of a colonoscopy is reduced by 3 percent to 6 percent. Top colonoscopists can reduce their patients' cancer risk by 82 percent.

> "...the plan is to take the software to the point where it can identify which polyps are benign and don't call for laboratory analysis and which do."

Promising new research at UC Irvine indicates that colonoscopies aided by artificial intelligence (AI) software can dramatically improve ADR, even among highly proficient colonoscopists. The research is being conducted by a team led by UCI Health gastroenterologist Dr. William E. Karnes, who is working with AI specialists at DocBot, a company that began through UCI Applied Innovation.

Essentially, all colorectal cancers start as a benign precancerous polyp, Karnes said. The most common of these are adenomas, which have a mean dwell time of 10-plus years to progress from normal tissue to colorectal cancer. Colonoscopy remains the gold standard for finding adenomas and is the only test capable of removing all adenomas found in the colon.

Karnes and Professor Pierre Baldi in the UCI Department of Computer Science first developed a proof-of-concept algorithm to spot signs of an adenoma, based on a database of polyp images that Karnes and his gastroenterology team assembled. The plan is to test it this summer in real time during colonoscopies, but the first round of testing involved the use of videos taken during previous colonoscopies and reviewed afterward.

"We had three experts at UCI with very high ADRs review the videos," said Karnes, director of the high-risk colon cancer program and of colonoscopy quality at UCI's H.H. Chao Digestive Disease Center. "We had them mark every polyp they saw. On first review, they found about 20 percent more polyps than the original colonoscopist had removed. Then they viewed it with an AI overlay; AI found all the polyps they had discovered, plus about 20 percent more polyps than even they did."

The software operates on a standard desktop machine, processing 98 images per second, which is nearly four times faster than required for live video.

The important next step is to test the software during actual colonoscopies. "We have to make sure the interface is absolutely perfect for real-time colonoscopy," Karnes said. "Once we've achieved that, we'll be ready to do our randomized study. We'll see — with the overlay and without it — if the AI increases the rate of polyp discovery."

If the software operates as expected, it will warn the colonoscopist during the procedure when it identifies tissue showing signs of being a polyp and should be removed. With such assistance, AI could bring all colonoscopists, including those with low ADR rates, to top ADR levels, and ensure that patients are getting a high-detection procedure no matter who their doctors are.

Eventually, Karnes said, the plan is to take the software to the point where it can identify which polyps are benign and don't call for laboratory analysis and which do. "It's expected that hundreds of millions of dollars of medical dollars could be saved if we could diagnose a polyp by looking at it," he said.

For more information, contact
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About us: Chao Family Comprehensive Cancer Center

UC Irvine Chao Family Comprehensive Cancer Center is Orange County's only National Cancer Institute-designated comprehensive cancer center. It is a vital resource for the people of Orange County and surrounding areas, generating and disseminating new knowledge about the causes, prevention and treatment of cancer, as well as training the next generation of cancer providers and caregivers, and alleviating the overall cancer burden on our population.

Located at UC Irvine Medical Center in the heart of Orange County, the Chao Family Comprehensive Cancer Center integrates research, prevention and the most advanced diagnostics, treatment and rehabilitation programs to provide the best possible care for patients and their families.

Gastrointestinal cancer specialists also see patients at the UCI Health H.H. Chao Comprehensive Digestive Disease Center offices in Orange, Tustin, Irvine, Costa Mesa and Corona.

Our cancer center researchers form disease-oriented teams that bring together patient-centered basic, translational and clinical investigators to facilitate the movement of discoveries through the pipeline into the clinical arena.

With a world-class, multidisciplinary team of surgeons, radiation oncologists, medical oncologists, pathologists, nurses, rehabilitation therapists, pharmacists, social workers and dietitians, the Chao Family Comprehensive Cancer Center is able to address cancers of all types and degrees of severity.

Contact us

To learn more about our cancer clinical trials or determine whether we have one that might meet your patients' needs, call the Chao Family Comprehensive Cancer Center at 877-827-8839 or email us at ucstudy@uci.edu