Ronald Salem, M.D., came to Yale Cancer Center 21 years ago to operate on patients with a wide range of cancers. But the longer he practiced, the more he found himself concentrating on patients with pancreatic cancer.

“I’ve really been fascinated by how poor the outcome in pancreatic cancer is and how we as surgeons can improve that outcome,” he explained. “Pancreatic surgery was once considered too risky for patients. It has become much safer over the last 10 years, with low mortality rates of about 1%.”

Pancreatic cancer remains one of the most difficult cancers to cure. But at Yale, an interdisciplinary team specializing in pancreatic cancer is creating hope for patients through innovative strategies: catching dangerous lesions before they become cancerous; making “inoperable” tumors operable through other therapies; and developing new drugs to improve outcomes.

“Perhaps what’s most exciting is the fact that we’re now able to identify patients with abnormalities of the pancreas that are going to become cancer,” Dr. Salem explained.

A Team Approach

Now the goal is to determine why this drug is working in patients like Maureen, and not in others. The Yale clinics and labs have joined forces and by collecting blood samples and tumor tissue from patients, they hope to be able to discover which patients should be treated using this anti-tumor drug, and develop new therapies for those it’s not working for. “I am excited about this drug for many reasons, but the main reason is because it is well tolerated by patients, the activity of the drug is remarkable, and the results seem to be long-lasting,” said Dr. GETTINGER.

“64% of those who are treated with this drug are still alive after four years,” said Dr. GETTINGER.

For Maureen, this discovery was a miracle. A trial of anti-PD-1 therapy initiated at Yale in five cancers: melanoma, kidney, prostate, colon, and lung. Maureen has been on the trial since June of 2010 and has shown a dramatic response to the therapy. At the time she entered the trial her prognosis was poor and her quality of life low. She had eight areas of metastatic disease involving her lung, kidney, liver, spleen, brain, and heart. Over a year later, all areas of disease have shown a substantial reduction in size and extent.

“While I would not say it’s a miracle to get people like Maureen to survive,” Dr. GETTINGER said, “over the last two weeks CT scan results and hope for the best. My disease is the last thought I have before sleep and my first thought in the morning, and I am blessed every day that I get to take this medicine. I just celebrated 39 years of marriage to my wonderful husband, saw my youngest daughter graduate from college, my oldest daughter get married, and the birth of twin grandsons. None of that would have been possible without the support of my family and the opportunity to be on this trial. For that I will always be grateful.”
Typically, those abnormalities first show themselves by chance, perhaps during a CT scan to find a kidney stone or to look into a lung infection.

“The doctors in our Interventional Endoscopy Program are world-class at identifying these lesions,” Dr. Salem said. By carefully evaluating the risk of a lesion becoming cancerous, they can recommend potentially lifesaving surgery while avoiding unnecessary operations.

Early imaging studies have tremendous benefits, but there is a hitch. “It’s not clear who to screen,” said Howard Hochster, MD. He is an oncologist who recently came to Yale to increase clinical trial opportunities for patients with advanced cancers, including pancreatic. A clear set of risk factors has not been identified for pancreatic cancer. That’s one of many examples of how knowledge about the disease is lacking. Dr. Hochster collaborates with doctors from many disciplines, as well as laboratory scientists, to develop more information, and therefore better weapons, against the disease.

One of the newer, and most effective, weapons used against pancreatic cancer is neoadjuvant therapy. “We cannot cure a patient if we can’t operate,” said Dr. Salem, who is the Lampman Professor of Surgery, but some tumors are inoperable. Traditionally cancers are treated first with surgery to remove the tumor, then with adjuvant therapies—such as chemotherapy and radiation—to deal with any cancer cells that may be left behind. Neoadjuvant therapy reverses the order. When a patient comes in with a tumor too extensive to remove, chemotherapy and/or radiation can be used to shrink the tumor to the point where a surgeon can excise it. Patients have the choice of standard chemotherapy or radiation therapies and increasingly of new therapies being offered through a growing number of clinical trials at Yale Cancer Center. Many of those trials are being spearheaded by Dr. Hochster, who became fascinated with clinical research as a student at the Yale School of Medicine, under the late Sterling Professor of Medicine and Epidemiology, Alvan Feinstein. “We’re trying to inject a degree of scientific rigor into clinical therapies,” remembered Dr. Hochster. Back in the 1970s, studies might consist of only 20 patients, with no control groups and little in the way of statistical analysis. Today, many volunteers participate in a single study, often at multiple sites, and controls and analysis are meticulous. It’s painstaking work that ultimately worthwhile. “It makes it possible to offer our own patients the newest therapies,” said Dr. Hochster.

He is currently investigating agents that may block the division of pancreatic cancer cells, which are notorious for their rapid growth. Dr. Hochster is also evaluating ways to deliver effective chemotherapy while reducing the side effects that patients experience. Together with radiation oncologist Peter Glazer, MD, PhD, he is looking into an antibody that could disrupt pancreatic cancer’s DNA and increase the effectiveness of radiation therapy. Finally, Yale’s extensive technical resources and expertise in genetics hold the possibility of developing “personalized” treatments that would target the exact molecular structure of an individual’s tumor. Patients are already enrolled in some clinical trials for new pancreatic therapies. Other therapies are still being fine-tuned in laboratories.

Dr. Salem was initially drawn to specialize in pancreatic cancer because of its often daunting prognosis. Physicians are still far from satisfied with the tools at their disposal, but the pancreatic team is able to offer patients new options that are leading to better outcomes. “Today there is more hope for our patients because of the extraordinary efforts of our teams.”

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Ronald Salem, MD

“Clinical trials developed at Yale make it possible to offer our own patients the newest therapies.”

Howard Hochster, MD