Patients may be referred by a medical professional, or may refer themselves, to Simmons Cancer Center’s pancreatic cancer programs. Patients with a pancreatic mass, pancreatic cyst, dilated pancreatic duct, or a high-risk condition for the development of pancreatic cancer should be referred for evaluation in these unique multidisciplinary programs.

Making a referral is easy – contact UT Southwestern Simmons Cancer Center’s patient intake specialist. Referrals are accepted both for patient care and second opinion consultations.

ph  214-645-0100
fax  214-645-9292
PANCREATIC CANCER

EARLY DETECTION
With that purpose, the Pancreatic Cancer Prevention Program at UT Southwestern and Harold C. Simmons Comprehensive Cancer Center has assembled a diverse team of experts from specialties including radiology, gastroenterology, surgical oncology, and cancer genetics. The group’s goals are to identify patients with known risk factors for pancreatic malignancies and to develop personalized plans of action. These plans include education and outreach; imaging of the pancreas and lifetime surveillance for abnormalities; sampling of tissue or cyst fluid; “banking” of biological samples for future reference or research; and surgery, if needed.

Patients treated and followed in the program have an elevated risk for developing pancreatic cancer due to:

- A family history of the disease, or of certain other malignancies that can be linked to pancreatic cancer risk
- Genetic testing showing mutations associated with an increased risk of the disease
- The presence of one or more so-called mucinous cysts within the pancreas, which typically behave in a benign manner but which can develop into a cancer over time

A proactive approach

A core component of the Pancreatic Cancer Prevention Program is ongoing assessment of such cysts for characteristics indicating that they have, or are likely to, become cancerous. Identifying cysts demonstrating signs of malignant degeneration allows surgeons to intervene early, before a cancer can develop or advance.

“Pancratic cancer is an absolutely devastating disease, and it’s because it’s typically not picked up until it’s too far gone,” says gastroenterologist and interventional endoscopist Dr. Nisa Kubiliun, Assistant Professor of Internal Medicine and Co-Director of the UT Southwestern Pancreatic Cancer Prevention Program. The pancreas, she notes, is situated deep in the belly, and a common symptom of pancreatic cancer – back pain – is not necessarily associated with the organ or considered cause for alarm. “This is part of the problem we face as clinicians; we end up finding the disease once it’s widely metastasized, when our treatment strategies are largely less effective.”

Although pancreatic cancer is on the rise – with new cases increasing 0.6 percent per year on average in the last decade – it is still relatively rare, so it’s ineffective to screen the general population for the disease, says Professor of Surgery Dr. Rebecca Minter, who co-directs the Pancreatic Cancer Prevention Program with Dr. Kubiliun. She adds, however, that “patients with identified precursor lesions to pancreatic cancer such as mucinous cysts, or an underlying genetic condition placing them at risk, represent an enriched patient population that we believe is effective to screen and surveil. Our greatest opportunity to intervene or cure pancreatic cancer is before it develops into an invasive cancer.”

“FINDING AND ASSESSING LESIONS

Radiologists often identify pancreatic lesions incidentally, typically on abdominal imaging performed for some other purpose, such as to investigate urgent medical problems in the emergency room or for follow-up of other cancers that may be under control, says Assistant Professor of Radiology Dr. Gaurav Khatri, lead radiologist for the Pancreatic Cancer Prevention Team.

“We’re still learning a lot about these lesions, which are common in the general population,” Dr. Khatri says. “They can grow very slowly and can continue to develop over multiple years. Until the last couple of years, they have not gotten a lot of attention, but now some experts are wondering whether they carry higher risk than previously thought.”

At Simmons Cancer Center, ensuring further assessment of cysts or other anomalies is baked into the system – radiologists embed specific
boilerplate language into the patient’s electronic medical record that flags the finding, provides referral and contact information for the Prevention Program, alerts program team members, and directs referring physicians to management guidelines for pancreatic abnormalities.

“If we didn’t have the Prevention Program, these patients might not get the correct follow-up from their referring physician,” Dr. Khatri notes.

The program’s close collaboration with radiologists to initiate follow-up care “is totally a game changer,” Dr. Kubiliun adds. “Now we capture every one of these patients and can continue to follow them and try to ensure that they don’t develop features that are worrisome for malignancy.”

ENTERING THE PROGRAM

Patients with a pancreatic cyst, as well as those who have a hereditary risk for pancreatic cancer, can be referred to the program. The Prevention Program’s first point of contact is its patient intake specialist, Naomi Chambell, who schedules patients and connects them with patient nurse navigator Chris Bishop, B.S.N., RN. Working closely with physician assistants Veronica Coleman, M.P.A.S., PA-C, Assistant Professor with the Department of Physician Assistant Studies, and Lan Vu, M.P.A.S., PA-C, Mr. Bishop reviews each patient’s medical and family histories, previous imaging, genetic tests, and details about any cysts that have been detected and whether symptoms are present in relation to these cysts. In addition, he answers any questions that a patient may have about the program and the purpose of surveilling pancreatic cysts.

Mr. Bishop also gathers patients’ records, imaging, and additional test results from other health care providers, making sure everything is on hand for specialists in the Prevention Program to review before a patient arrives for a consultation. Any needed procedures, such as endoscopic ultrasound or additional imaging, are scheduled in the interim, and appointments are set with the specific providers each patient needs to see. Mr. Bishop also coordinates patients’ care on the day of their visit, helps put the specialists’ recommendations into action, and remains the primary contact for questions and follow-up.

To help assess patients with a pancreatic lesion, both initially and in follow-up surveillance, UT Southwestern has a dedicated group of about a dozen abdominal radiologists who use state-of-the-art imaging techniques designed to better capture changes within the lesion, pancreatic duct, or the remainder of the pancreas parenchyma (the functional portion of the organ), Dr. Khatri says. Those techniques include magnetic resonance (MR) cholangiopancreatography and additional dedicated high-resolution MR imaging sequences looking for the earliest signs of pancreatic cancer within the gland.

“The radiologists associated with the Prevention Program are accustomed to looking for findings that a general radiologist might not be attuned to looking for,” Dr. Khatri says. For instance, the radiologists note whether a cyst, which is normally fluid-filled, has developed solid material or septations in its interior; whether the septations have changed since the prior examination; if its walls are thick, or “nodular”; or whether the pancreatic duct is obstructed or dilated.

PROBING MORE DEEPLY

To further help determine risk, or to establish a diagnosis, a patient might also undergo an endoscopic ultrasound. For the procedure, Dr. Kubiliun uses a long, thin camera with an ultrasound probe embedded on the tip of the scope, which is passed through the mouth and esophagus and into the stomach and small intestine. From there, the pancreas can be visualized, and cysts or other lesions, including possible cancers, can be sampled in a minimally invasive manner.

Extracted samples – typically fine-needle aspirates – allow physicians to more closely assess cyst fluid for molecular markers or other precancerous features, offering added clarity about the biologic behavior of a pancreatic cyst. Endoscopic ultrasound also can sample solid pancreatic masses to see whether tumor cells are present and, if so, to determine the type of tumor the lesion represents. (If
a lesion turns out to be cancerous, the patient is referred to the Pancreatic Cancer Multidisciplinary Program for treatment.)

THE SEARCH FOR BIOMARKERS

With patients’ consent, samples of fluid extracted from cysts, along with blood samples and detailed information about how each case unfolds, are being banked in a biorepository for future research. Such research might examine, for instance, whether there’s some biological clue, or marker, in the fluid or blood that might help predict who will go on to develop pancreatic cancer.

Finding biomarkers that suggest who is likely to develop cancer will bring new precision to the process of determining which at-risk patients truly need surgery for a pancreatic lesion, says surgical oncologist Dr. Adam Yopp, Associate Professor of Surgery and Medical Director of the Simmons Cancer Center Tissue Management Shared Resource. So far, no such biomarkers have been validated for pancreatic cysts, he says: “It’s all investigational right now.”

Doing the research needed to identify pancreatic cancer biomarkers is likely to require collaboration among multiple institutions, Dr. Yopp adds. “The reality is that to do any of these studies we’ll need thousands and thousands of patients. Collecting these samples positions us to work with other institutions to identify predictors of progression to pancreatic cancer.”

CUSTOMIZED CARE

Once imaging and testing are completed, each individual case is reviewed in the Prevention Program’s Multidisciplinary Conference, where radiologists, gastroenterologists, surgical oncologists, and genetic counselors meet in order to decide the best next steps for care. The conference includes the same group of experts reviewing each person’s case over time, relying on imaging that is consistently acquired from visit to visit — allowing for, as Dr. Minter says, “apples-to-ap-
While there are no formal, validated screening guidelines for pancreatic cysts, the multidisciplinary group, using an evidence-based approach, works in concert to determine each patient’s risk level, then reaches a consensus on an individualized course of action for that patient. “It’s not a one-size-fits-all approach,” Dr. Kubiliun says.

If a cyst or other lesion appears worrisome, the Prevention Program’s experts will carefully weigh potential risks versus benefits. In some cases, the team may recommend excision. In other instances, long-term surveillance with a shorter interval between imaging might be advised.

Patients with elevated risk for pancreatic cancer due to certain genetic predispositions might also undergo regular MRI surveillance in search of new or growing lesions. Over time, some patients might have no changes while others have rapidly developing change and still others have a previously dormant aberration that suddenly becomes active.

“Ideally we’d catch any lesions — if not prior to tumor formation, then in the very early stages,” Dr. Kubiliun says, adding that because MRI does not involve radiation, such surveillance is safe over the long term.

Parkland Health & Hospital System, Dallas County’s safety net health care provider and the primary teaching facility for UT Southwestern, is developing similar cyst follow-up and other prevention services through its Multidisciplinary Pancreas Clinic. Biological samples from that clinic also are banked at UT Southwestern.

THE RISKIEST CYSTS

Pancreatic cysts grow increasingly common with age; as many as one-quarter of patients over age 65 have them. While most are benign, two types of mucinous cysts are more prone to develop into cancer. Intraductal papillary mucinous neoplasms, or IPMNs, can affect the entire pancreas, sometimes necessitating complete removal of the organ to excise all at-risk tissue, Dr. Minter says. More commonly, only portions of the pancreas are involved, although ongoing surveillance is required because the growths might recur elsewhere in the organ. By contrast, mucinous cystic neoplasms, or MCNs, are unifocal (single-site), and following surgical resection do not require ongoing surveillance of the remaining pancreas.

Besides structural features of a cyst, decisions to operate hinge on the presence of symptoms such as pancreatic inflammation (pancreatitis) or difficulty eating. And cysts greater than 3 centimeters warrant closer attention.

“Only a small number of patients with pancreatic cysts need an opera-
As many as 10 percent of pancreatic cancers are thought to result from inherited mutations, although only about one-fifth of those genetic causes have been pinpointed. Hereditary syndromes linked to pancreatic cancer are associated with other cancers as well (see image below). For instance, mutations in the BRCA1 or BRCA2 genes – which can underlie breast and ovarian cancers – are also associated with exocrine pancreatic cancer, the predominant form of the disease.

“These different cancers can be so important,” Ms. Watson says. “People think, ‘I don’t have a family history of pancreatic cancer,’ but that’s not the only cancer that matters here.”

Where appropriate, genetic testing is recommended for mutations in more than a dozen genes linked to pancreatic cancer, plus a handful associated with hereditary pancreatitis, which can also predispose patients to developing cancer. Patients found to have a hereditary risk are counseled on lifestyle changes, such as quitting smoking, that can help reduce their odds of developing pancreatic cancer.

For patients with hereditary syndromes, proven surveillance techniques can be implemented for those other cancers, such as mammography or breast MRI for people with BRCA mutations, colonoscopy in connection with a condition known as Lynch syndrome, and skin cancer screenings for patients with familial atypical multiple mole melanoma (FAMMM) syndrome. Such patients also are counseled on prevention strategies, such as sun safety precautions for FAMMM syndrome, Ms. Watson says. And the genetic counseling team will guide patients on how to talk to family members about also getting tested for mutations.

“We’re available as a support resource for patients throughout the whole process,” Ms. Watson says. Since the launch of UT Southwestern’s Pancreatic Cancer Prevention Program in January 2016, more than 350 patients with increased risk for pancreatic cancer have been evaluated. Two-thirds of these patients were referred for cystic neoplasms of the pancreas and approximately one-third for high-risk hereditary conditions. Through this program, patients have been found to have previously unknown germline mutations predisposing them to pancreatic cancer, as well as high-risk lesions, which were successfully resected prior to development of pancreatic cancer. The next step in preventing this disease is identification of biomarkers that can predict which patients are at highest risk, and programs such as this one will provide a platform for that critically important work.

Across medical specialties, integrated support and guidance for at-risk patients at every opportunity is what distinguishes UT Southwestern’s Pancreatic Cancer Prevention Program in the fight against the disease. “There are only a handful of pancreas programs around the country similar to this one, where radiologists, gastroenterologists, surgical oncologists, and other team members work together so closely,” Dr. Khatri says.
The risk of pancreatic cancer increases with age. Men and African-Americans of both genders have a slightly elevated risk of developing the disease. Other potential risk factors are:

- Being overweight or obese
- Smoking and use of smokeless tobacco
- Exposure to chemicals in dry cleaning and metalworking industries
- Infection of the stomach with the ulcer-causing bacterium *Helicobacter pylori*
- Chronic pancreatitis (inflammation of the pancreas)
- Cirrhosis (scarring) of the liver
- Type 2 diabetes
- Being overweight or obese
- Smoking and use of smokeless tobacco
- Exposure to chemicals in dry cleaning and metalworking industries
- Infection of the stomach with the ulcer-causing bacterium *Helicobacter pylori*
- Chronic pancreatitis (inflammation of the pancreas)
- Cirrhosis (scarring) of the liver
- Type 2 diabetes
A family history of pancreatic cancer can increase risk of the disease, as can certain hereditary cancer predisposition syndromes.

**THOSE SYNDROMES INCLUDE:**

- **Hereditary breast and ovarian cancer syndrome** ([BRCA1/BRCA2 gene mutations]), which is associated with an increased risk for breast, ovarian, pancreatic, melanoma, and prostate cancers

- **Lynch syndrome** ([MLH1, MSH2, MSH6, PMS2, and EPCAM mutations]), which is associated with higher risk of a number of malignancies, including colorectal, uterine (endometrial), stomach, ovarian, small bowel, pancreatic, urinary tract, and central nervous system cancers

- **Familial atypical multiple mole melanoma syndrome** ([CDKN2A mutations]), which is linked to an increased risk of melanoma and can also be associated with an increased risk of pancreatic cancer

- **Familial pancreatitis** (typically [PRSS1 mutations])

- **Peutz-Jeghers syndrome** ([STK11 mutations]), which is associated with an elevated risk for cancers or polyps of the gastrointestinal tract, as well as pancreatic, breast, and certain types of cervical or ovarian cancer

- **Von Hippel-Lindau syndrome** ([VHL mutations]), which is associated with noncancerous tumors of the brain, spinal cord, and retina, as well as kidney cancer, pheochromocytomas, pancreatic neuroendocrine tumors, and pancreatic cysts

**OTHER GENES, SUCH AS PALB2 AND ATM, HAVE ALSO BEEN LINKED TO AN INCREASED RISK OF PANCREATIC CANCER. INDIVIDUALS SHOULD CONSULT WITH A CANCER GENETICS COUNSELOR IF SOMEONE IN THE FAMILY HAS BEEN DIAGNOSED WITH A HEREDITARY CANCER PREDISPOSITION SYNDROME, MORE THAN ONE TYPE OF CANCER, OR IF PANCREATIC CANCER HAS OCCURRED IN:**

- Several members of the same or multiple generations of a family

- At least two generations on the same side of the family

- Family members who were diagnosed at an age younger than 50
Pancreatic cancer is difficult to detect because few symptoms are noticed early in the course of the disease. Symptoms that do arise are similar to those of other diseases and should be evaluated by a physician.

**SYMPTOMS**

**SYMPTOMS OF THE MOST COMMON FORMS OF THE DISEASE – EXOCRINE PANCREATIC CANCER OR PANCREATIC ADENOCARCINOMA – INCLUDE:**

- Jaundice (yellowing of eyes and skin; dark urine; pale or gray stools)
- Pain in the upper abdomen or mid-back
- Sudden onset or worsening of existing diabetes, especially in patients who lack risk factors for the condition
- Poor appetite
- Unexplained weight loss
- Nausea, vomiting
- Digestive discomfort, such as a burning sensation or bloating in the abdomen
- Pancreatitis without clear cause
- Blood clot in a large vein, such as in the leg, developing for no clear reason

**PANCREATIC NEUROENDOCRINE TUMORS, WHICH ACCOUNT FOR ONLY ABOUT 5 PERCENT OF PANCREATIC TUMORS, CAN BE BENIGN OR MALIGNANT. TUMORS THAT ARE MALIGNANT CAN CAUSE SIMILAR SYMPTOMS TO PANCREATIC EXOCRINE CANCER.**

The majority of neuroendocrine tumors are classified as nonfunctioning; however, some are functional and can release an excess of various hormones into the bloodstream, causing hormone-related symptoms such as:

- Abdominal pain
- Diarrhea
- Acid reflux
- Peptic ulcer disease
- High or low blood sugar
- Electrolyte abnormalities
PANCREATIC CANCER

PRECISION CARE
Exocrine pancreatic cancers, the predominant form of the disease, can be classified based on whether they might be surgically removed, or have spread to distant organs:

**RESECTABLE CANCERS** are those that are confined within or have limited extension beyond the pancreas. Surgery is typically performed with chemotherapy given afterward. Radiotherapy may also be used to reduce the risk of recurrence. In addition, research is testing whether chemotherapy given before tumor resection can improve patient selection for surgery as well as long-term outcomes.

**BORDERLINE RESECTABLE TUMORS** may be near structures such as major blood vessels located near the pancreas, which would make tumor removal more complicated. These tumors are often treated with chemotherapy and radiotherapy first, in an effort to reduce their size and improve the odds of a successful surgery.
LOCAL ADVANCED CANCERS have not spread widely but may be entangled with important blood vessels that cannot be safely resected or easily reconstructed, making it very difficult or impossible to safely remove the tumors in full. With chemotherapy administered first to try to shrink the cancer – plus recent advances in surgery – some such tumors may still be operable, especially in the hands of a surgeon who is skilled in the reconstruction of these major blood vessels. In addition, radiotherapy is sometimes used. Surgery might also be performed to help address specific symptoms caused by a tumor.

METASTATIC CANCERS are those that have spread to distant organs and cannot be completely removed. Chemotherapy is the main treatment option. Surgery, radiotherapy, or other interventions might be performed to alleviate symptoms.
A SINGLE POINT OF ENTRY.
Referrals are made through the pancreatic cancer programs’ patient intake specialist. The intake specialist is the sole point of entry for both the Multidisciplinary Pancreatic Cancer Program (for treatment of pancreatic cancer or other pancreatic tumors) and the Pancreatic Cancer Prevention Program (for patients with a finding of a pancreatic cyst, or a genetic or family history that increases their risk for pancreatic cancer).

COORDINATION AND PREPARATION.
After the patient intake specialist schedules the appointment, the programs’ patient nurse navigator will collect necessary records and test results; determine logistical needs for patients coming from out of town; ask patients about symptoms, medical and family history, and previous genetic testing; schedule any additional testing or imaging as required; and build a case file.

A ONE-STOP CLINIC.
After each patient file undergoes a preliminary review, the patient nurse navigator will schedule a one-day clinic visit. At that visit, the patient will have appointments lined up with the various specialists needed for comprehensive preventive care or cancer treatment, with necessary tests scheduled and a treatment plan provided at the conclusion of the visit.

Preventive Care

A PROACTIVE PLAN.
Specialists in radiology, gastroenterology, and surgical oncology meet the same day of the patient’s clinic visit to evaluate each case and develop a plan of care that may include further testing or continued surveillance. In the case where a pancreatic cyst has worrisome features, surgery may be recommended. The patient navigator arranges all necessary follow-up steps, either at UT Southwestern or through other providers, if needed, such as for out-of-town patients.
COMMUNICATION WITH OTHER PROVIDERS.
Details of each patient’s cancer care plan, treatment, and follow-up recommendations developed over the course of therapy are routinely communicated to the patient’s primary care and referring physician.

SUPPORT AND MORE.
As part of the one-day visit, cancer patients and their caregivers are invited to take part in a lunchtime Patient/Family Support Session, which outlines a wide range of community and UT Southwestern support services and resources.

CANCER GENETICS REVIEW.
Certified genetic counselors review patients’ personal and family histories for any suggestion of a hereditary condition that may be contributing to their cancer, and referral for formal genetic counseling (including possible testing) is arranged as appropriate.

CLINICAL TRIAL EVALUATION.
All patients evaluated in the program are also screened by the research team to see whether the patient is a candidate for a clinical trial at UT Southwestern.

MULTIDISCIPLINARY CANCER CARE.
On the same day each patient is meeting with the necessary cancer care providers, his or her case is reviewed—and a treatment plan is developed—by the Multidisciplinary Program’s Pancreatic Cancer Tumor Board, a conference of specialists in medical, surgical and radiation oncology, radiology, cancer genetics, and clinical research.
MULTIDISCIPLINARY TREATMENT

Cancer of the pancreas is a uniquely challenging disease. Yet medical science is beginning to make progress in the fight against it, with new medical therapies and approaches, and surgical and radiotherapy advances.

UT Southwestern physicians are battling pancreatic cancer on multiple fronts, with the goal of improving not just patient survival, but personal well-being. In the Simmons Cancer Center’s Multidisciplinary Pancreatic Cancer Program, the battle starts with the logistical support that is needed to ensure that every needed specialist can evaluate each patient promptly and thoroughly in just one day.

These specialists – nationally and internationally recognized experts in the medical, surgical, endoscopic, and radiotherapy tactics deployed against pancreatic cancer – develop a strategy that is tailored individually for each patient and his or her disease. As treatment progresses, that plan is revised or adapted, as circumstances warrant, by the same expert group. And from the outset, a team of supportive care professionals and volunteers is available to help patients cope with their cancer and its physical and emotional complications.

“What’s unique about our program is that it is truly interdisciplinary and integrated. We triage patients, determine everything they need, connect them with multiple specialists, and formulate and facilitate their treatment plan so they can begin treatment the very next week,” says Dr. Rebecca Minter, Surgical Director of the Multidisciplinary Pancreatic Cancer Program. “Otherwise they can end up with all of these parallel and sequential appointments, like being referred to a medical oncologist after a surgeon, then requiring additional tests, then needing a port placed for their chemotherapy – and the next thing you know it has been several weeks before they actually start their treatment.

“And obviously, with pancreatic cancer, time is of the essence.”

UT Southwestern physicians apply the same approach in their care of pancreatic cancer to patients at Parkland Memorial Hospital, Dallas County’s safety net care provider and the University’s primary teaching facility.

IN UT SOUTHWESTERN’S MULTIDISCIPLINARY PANCREATIC CANCER PROGRAM, PATIENTS BENEFIT FROM:

- Expedited testing and imaging at onsite facilities, with standardized radiology reports to ensure that patients’ tumors are precisely staged
- Same-day development of a personalized treatment plan by the program’s multidisciplinary Tumor Board
- Expertise in a range of complex surgical procedures, including minimally invasive operations that can speed patient recovery, as well as complicated vascular reconstructions required to remove some tumors
- The latest evidence-based chemotherapy, radiation, and combination treatment strategies
- Access to novel immunotherapy treatments through Simmons Cancer Center’s robust clinical trials program
- Proactive symptom management
- Genetic counseling and testing, where appropriate
- Cutting-edge UT Southwestern facilities and technology
- Oncology-certified nurses and other professionals with expertise in cancer care
- Easy access to experts in social work, nutrition, and music therapy who work regularly with pancreatic cancer patients, along with cancer-specific support from specialists in physical rehabilitation, psychology, and palliative care
- The opportunity to have specimens stored for ongoing and future research

The comprehensive, coordinated care provided in the Multidisciplinary Program begins with one phone call to the patient intake specialist. From that point, a multitude of needs – procuring medical records and previous imaging; arranging for additional testing, biopsy, or port placement; facilitating travel for patients from out of town; and coordinating care with hometown physicians – are anticipated and managed by the Multidisciplinary Pancreatic Cancer Program’s Multidisciplinary Tumor Board.
Program’s patient nurse navigator, in collaboration with the program’s physician assistants.

“One of the biggest things patients are experiencing when they call us is a significant amount of anxiety, whether it’s a new diagnosis (of pancreatic cancer) or they’re coming for a second opinion because their first therapy isn’t working,” says Lan Vu, M.P.A.S., PA-C, physician assistant for the Division of Surgical Oncology. “That first contact tells patients, ‘We’re here for you, we’re giving you our undivided attention, and we’re already looking at your case now rather than just when you come for your first visit,’” she says.

**SPECIALISTS AT THE READY**

The first clinic visit is designed so that physicians come to the patient, rather than the patient bouncing from one location to another. After the day’s appointments are completed, the full range of specialists in the Multidisciplinary Program meets, along with other professionals, as part of the Pancreatic Cancer Tumor Board.

Discussing and debating the details of each case, the board develops a consensus on the best plan of action for cancer treatment and related care. Instead of having to piece together a picture of their treatment from multiple specialists, patients at UT Southwestern leave the one-day clinic with a treatment plan in hand. That plan, along with treatment updates, is communicated to referring and primary care physicians.

“Everyone at the Tumor Board meetings has input on each patient,” says Associate Professor of Radiation Oncology Dr. Jeffrey Meyer, who specializes in pancreatic cancer and other gastrointestinal malignancies. “It’s truly multidisciplinary input. There are going to be unique aspects to everyone’s case, so that’s why multidisciplinary input is essential.”

A key task of the board is to first classify each person’s cancer as metastatic or nonmetastatic, then further determine which of the nonmetastatic cancers appear resectable (versus borderline resectable, locally advanced, or currently unresectable. From there, the team develops an individualized plan, says Multidisciplinary Program Medical Director Dr. Muhammad Shaalan Beg, who is also Medical Director of the Simmons Cancer Center Clinical Research Office. “It is essential to take time and understand what the goals of care are – not just the medical team’s goals, but the patient’s goals. Fifty to 60 percent of the time we tweak ‘textbook’ approaches for some personal reason, which is directly related to the patient,” he says.

“Developing a consensus on each case is important both for seamless care and patients’ peace of mind. It’s very important to set the expectations for patients up front,” Dr. Beg says. “Patients leave knowing what their cancer is, how we approach that cancer, and they get the same message from every surgeon, every medical oncologist, and every radiation oncologist they see.”

At the same time the Tumor Board is reviewing cases, another expert team – comprising supportive services professionals, along with a volunteer from the Dallas-Fort Worth affiliate of the Pancreatic Cancer Action Network
-- is conducting the program’s Patient/Family Support Session. The session supplies information about the supportive care services that the Cancer Center and the Pancreatic Cancer Action Network have to offer, allowing patients and their caregivers to access important adjuncts to treatment when they are needed. These services can include minimizing the side effects of treatment, providing effective pain management strategies, and offering guidance regarding optimal nutrition and food choices.

“Pancreatic cancer has a significant emotional impact,” Dr. Minter says. “The Patient/Family Support Session is designed to ensure that patients have much more than just their medical needs met. Our goal for patients is a longer quantity of life and a better quality of life.”

A FULL RANGE OF CARE

The Multidisciplinary Program features specialists from multiple medical and oncology disciplines who focus exclusively on pancreatic and other gastrointestinal cancers to expeditiously address issues specific to each patient. For instance, individuals with a newly identified pancreatic mass might see gastroenterologist Dr. Nisa Kubiliun, who specializes in interventional endoscopy.

In a procedure known as endoscopic ultrasound (EUS), Dr. Kubiliun guides a thin tube into the mouth and down into the stomach and first part of the small intestine. At the tip of the tube is a small ultrasound probe that emits sound waves. The sound waves bounce off surrounding structures, such as the pancreas, bile ducts, and liver, and are recaptured by the probe and converted into black-and-white images that the physician interprets. Because it sits next to the stomach and small intestine, the pancreas can be imaged in great detail with EUS.

Pancreatic tumors also can be biopsied in a minimally invasive way via EUS in order to establish a diagnosis. Another endoscopic procedure, ERCP (endoscopic retrograde cholangiopancreatography), is used to address a common pancreatic cancer complication, jaundice, which can result from an obstructed bile duct. “An obstructed bile duct leads to a variety of different problems: infection, malabsorption (of nutrients), fatigue, and inability to receive some chemotherapy agents,” notes Dr. Kubiliun. ERCP can be used to diagnose the site of obstruction, image the problem in anticipation of surgery, or to place a stent to relieve blockage of the biliary tree. Stenting can alleviate the obstruction, help improve liver function, and perhaps allow for additional treatment such as chemotherapy or surgery, Dr. Kubiliun says.

“Fewer than 20 percent of patients have operable pancreatic cancers at the time of diagnosis, and we know only surgery can offer a chance for cure,” notes Dr. Minter. But pancreatic cancer is unique, and notorious, in that a large proportion of cancers come back after surgery. Offering treatment — chemotherapy and/or radiation — before surgery can increase the chance of a successful operation.

That highlights the importance of strong collaboration across disciplines to provide a full range of therapies for the treatment of pancreatic cancer — attacking it from multiple angles. Chemotherapy, a systemic therapy that circulates in the bloodstream, is used to treat patients with metastatic cancers. It also can treat microscopic tumor implants that have not yet grown big enough to be visualized, providing additional treatment.

“Developing a consensus on each case is important both for seamless care and patients’ peace of mind. It’s very important to set the expectations for patients up front.”

—Muhammad Beg, M.D. Multidisciplinary Program Medical Director
following surgery, or it may shrink a tumor before an operation – rendering a more advanced tumor more easily resectable.

Radiation therapy is a third treatment strategy that can be used to treat tumors that cannot be resected, or as an adjunct before or after surgery. How these treatments are sequenced depends on each patient’s unique scenario.

SURGICAL SKILL

UT Southwestern’s surgical oncologists are among the most experienced in the United States, skilled in performing an array of intricate procedures. This expertise is evidenced in the fact that they outperform peer institutions with respect to perioperative mortality for pancreatectomy as measured by Vizient, the University Hospital Consortium, and perform in the top 20 percent of institutions as measured by the National Surgical Quality Improvement Program (NSQIP). “One of the advantages of our approach at UT Southwestern is that every patient is guaranteed to see an expert in his or her particular disease,” says Associate Professor of Surgery Dr. John Mansour, a surgical oncologist in the Multidisciplinary Pancreatic Cancer Program. “We have the depth of talent among our surgeons to make sure that each patient is cared for by someone who has the most contemporary, patient-centered, and innovative approach available.”

This allows the surgical team to provide the approach best suited for each individual case and to minimize complications. Surgeons on the team perform high volumes of potentially curative operations, including the complex Whipple procedure (the most common surgery to remove tumors in the head of the pancreas). The team also has expertise in minimally invasive – robotic and laparoscopic – pancreatectomy, an approach that can facilitate a faster recovery.

“If you have pancreatic cancer, it’s critical that you go to a high-volume center that takes care of a lot of patients with pancreatic cancer,” Dr. Minter says. “Surgeons’ expertise, as evidenced by a high volume of cases, has been demonstrated to equate with improved surgical outcomes.”

Recent surgical advances are making it safer for pancreatic cancer patients with more advanced, delicately situated cancers to undergo tumor resection. UT Southwestern is one of just a handful of institutions in Texas that is skilled in these complicated operations, which can require removal and reconstruction of major blood vessels near the pancreas. “This means that a tumor that someone else may deem unresectable may actually be resectable, and we can resect it,” Dr. Minter says.

One of the most important steps a surgeon caring for a patient with cancer can make is to pause and consider nonsurgical aspects of care. “A critical aspect of planning surgery is the participation in planning of all phases of care, including chemotherapy and radiation,” Dr. Mansour says. “At UT Southwestern, we stress the importance of collaboration with the rest of the oncology team in order to get the best results for our patients. Often that means shrinking the tumor with chemotherapy or radiation prior to removing it. Combining treatments in that way can lead to faster recovery and improved patient survival.”

CHEMOTHERAPY EXPERTISE

For the vast majority of pancreatic cancer patients, chemotherapy plays a vital therapeutic role. In metastatic disease, the stage at which nearly half of cases are diagnosed, chemotherapy is used almost exclusively as a primary treatment and can help stabilize a cancer and extend patient survival.

Combination chemotherapies have been found to lengthen patient survival and improve well-being compared with previously used treatments, says Dr. Beg, a medical oncologist.

“More cancers are shrinking; more patients are living longer with better disease control and quality of life,” he says.

In patients with borderline resectable or locally advanced cancers, treatment with drug regimens, sometimes followed by a separate combination of chemotherapy and radiation, may be used in an effort to shrink a tumor, pulling it away from major blood vessels to make surgery possible.
viable and to improve the odds of a complete resection. Hence, more and more pancreatic cancers are becoming operable.

Studies have suggested that when these combination chemotherapies are used, “even if we don’t see a response on imaging, we can still frequently achieve a negative [tumor] margin for those patients,” Dr. Minter says. “That has really changed how we think about patients with borderline or locally advanced tumors, and we are more willing to take them to surgery following chemotherapy or chemoradiotherapy.”

In patients whose cancers appear resectable from the start, follow-up chemotherapy is generally administered. And researchers at Simmons Cancer Center and elsewhere are testing whether chemotherapy given to these patients additionally before surgery might improve long-term cancer control—without the delay in initiating any chemotherapy that currently occurs while a patient recovers from an operation.

Outside the clinical research environment, administering chemotherapy first for resectable cancers is considered at UT Southwestern on a case-by-case basis, Dr. Beg says. “The only reason we can do this is our multidisciplinary team can discuss options thoroughly for each patient and get buy-in,” Dr. Beg says. If it turns out such a cancer is no longer resectable after a couple of months of chemotherapy, doctors know that surgery would have been unlikely to stop the cancer to begin with and the patient is spared big operation, he adds.

IN SEARCH OF BETTER MEDICINES

Patients in the Pancreatic Cancer Multidisciplinary Program are continually evaluated for clinical trials. Trial coordinators attend the weekly Tumor Board meetings, noting which patients are eligible for trials open at Simmons Cancer Center.

“At UT Southwestern, we have the advantage of working with top-notch scientists who are at the cutting edge of basic science discoveries,” says Dr. Beg, who is principal investigator for multiple studies testing medicines for pancreatic and other GI cancers. “These scientists are leading studies to understand the molecular makeup of pancreatic cancer, and developing drugs to target those changes. Such discoveries are being tested in clinical trials at the Simmons Cancer Center.

“The Multidisciplinary Pancreatic Cancer Program allows us to find the right patient for the right trial. We can then expose our patient’s cancer to drugs that may not be available in the market for many years. At the same time, we learn how to advance these drugs in the battle against pancreatic cancer.”
The number of new cases of pancreatic cancer, unlike other cancers, is on the rise. Yet science has a lot of catching up to do in developing medical therapies for pancreatic cancer compared with, say, lung or breast malignancies. “A pancreatic cancer patient has one or two choices; a breast cancer patient has many, many more,” says Dr. Beg, who is part of the National Cancer Institute’s (NCI) Pancreatic Cancer Task Force, which makes recommendations for clinical trial planning.

Clinical trials at UT Southwestern frequently are initiated by the University’s own faculty, based on their scientific discoveries, with principal investigators who participate in numerous national trials. Simmons Cancer Center’s pancreatic cancer investigators regularly present their findings in leading journals and conferences. As an NCI–designated Comprehensive Cancer Center, Simmons has opportunities to open clinical trials supported by that agency or by collaborators in the pharmaceutical industry, which are frequently paradigm-defining studies. That’s important to patients because “it shows that our teams are broad as well as deep,” Dr. Beg says, describing a collaboration involving noted UT Southwestern diabetes researcher Dr. Philipp Scherer. The work is shedding new light on how diabetes that develops due to pancreatic cancer differs from diabetes in the broader population. Such an insight might someday help in screening for pancreatic malignancies or make chemotherapy more effective by incorporating an existing diabetes medicine. “We are able to understand the processes that are driving these cancers,” Dr. Beg says.

Scientists at UT Southwestern are leading a multipronged approach to understand how to best treat patients with pancreatic cancer. Research includes trials of two new chemotherapies for pancreatic cancer. One, a phase I trial, is testing a drug called beta-lapachone that was developed in research led by Simmons Cancer Center Associate Director of Translational Research Dr. David Boothman. Beta-lapachone was initially discovered in the bark of the Pau d’Arco tree and then chemically synthesized. Dr. Boothman has shown that the drug is activated by an enzyme present on cancer cells and makes hydrogen peroxide, which damages DNA and kills the pancreatic cancer cell. The activating enzyme, called NQO1, is not present in non-cancer cells, which are spared.

To explore this strategy in clinical trials, Dr. Boothman and Dr. Beg have been awarded a series of grants by the Pancreatic Cancer Action Network and have published their findings in highly regarded journals. Most importantly, these clinical trials have a robust strategy to send patients’ tumor tissue back to the laboratory to understand why, or why not, the drug is working.

It’s essential to have a pipeline of trials to test various strategies, says Dr. Beg, noting that such work – which translates findings from the laboratory to the clinic, and then back to the laboratory – requires a high degree of coordination and leadership. That’s possible only in Comprehensive Cancer Centers, where collaboration between multiple disciplines is woven into the fabric of the institutional culture, he says.

THE ROLE OF RADIATION THERAPY

Radiotherapy can play a role in pancreatic cancer at any stage, although how best to deploy it at different stages can be a subject of debate. “Radiation has a long history of use in pancreatic cancer, but it’s certainly not a black-and-white issue,” says Dr. Meyer.

In patients with metastatic cancers, radiotherapy may help alleviate pain caused by the primary tumor or metastases. For borderline resectable cancers, the goal of radiation – usually administered up front in combination with chemotherapy – is to enhance the likelihood that surgery can follow and that negative tumor margins may be achieved, Dr. Meyer says. “We’re trying to get these patients to the OR;” he says. “For me, it makes sense to ‘throw the kitchen sink’ at the tumors to enhance the likelihood that we will get a margin-negative surgery.” A conventional course of radiation is given daily on weekdays for 5½ weeks. However, Simmons Cancer
Center researchers are also experimenting with shorter courses (and more concentrated doses) that are delivered with a radiotherapy technique called stereotactic ablative radiotherapy or stereotactic body radiation therapy (SBRT), in which a total of just five treatments are given. In pioneering research at UT Southwestern, SBRT has proved to be a powerful tool in fighting other cancers such as lung cancer.

For patients with resectable cancers, use of radiotherapy differs from center to center. At UT Southwestern, “in general, we will consider radiation in someone who’s had an operation and completed adjuvant chemotherapy, to try to reduce the risk of cancer coming back locally,” Dr. Meyer says. Radiotherapy would likely not benefit patients whose cancers metastasize during or soon after chemotherapy, he notes.

The use of radiotherapy also varies in patients with locally advanced pancreatic cancers. Generally at UT Southwestern, those patients will start with chemotherapy and be continually re-evaluated, depending on their individual circumstances. “If they’ve been on chemotherapy for a long time, sometimes toxicities arise, and we may switch them to chemoradiotherapy,” Dr. Meyer says. SBRT’s short course of treatment doesn’t interfere with the ability to resume full-strength chemotherapy quickly, he adds. UT Southwestern is participating in a multi-institutional clinical trial testing chemotherapy with a regimen called FOLFIRINOX versus FOLFIRINOX then SBRT then a return to chemotherapy in patients with locally advanced, unresectable cancers.

In the future, pancreatic cancer patients may benefit from an entirely new type of radiotherapy, called carbon ion therapy. Like cutting-edge proton therapy, carbon ion therapy appears to be containable to targeted sites, rather than delivering radiation to healthy tissue too, as conventional X-ray beams do. Carbon ion radiation may also be more potent at killing cancer cells than comparable proton doses are. “There’s a lot of interest in carbon ion for both the physics and the biological aspects of it,” Dr. Meyer says.

Because carbon ion therapy is not yet available in the United States, UT Southwestern – in an effort driven by Associate Professor of Radiation Oncology Dr. David Sher – is partnering with institutions in Japan and Europe to compare the new therapy with conventional X-ray radiotherapy. Local patients in the study who are selected to receive carbon ion therapy would receive treatment overseas.

**BANKING FOR THE FUTURE**

Patients undergoing treatment at UT Southwestern are also invited to allow their blood and tissue samples to be used for research. Scientists are searching for biological markers that may help predict which pancreatic cancer patients are more likely to respond to specific therapies, as well as markers that could help monitor tumor response during treatment or detect a recurrence quickly, says Dr. Adam Yopp, Assistant Professor of Surgery.

“It’s kind of the holy grail in cancer, to figure out which biomarkers are predictive,” says Dr. Yopp, a surgical oncologist in the Multidisciplinary Pancreatic Cancer Program and Medical Director of the Simmons Cancer Center Tissue Management Shared Resource. “Right now, unfortunately, it’s all really at the research level.” A blood test now used to evaluate disease status in pancreatic cancer is a far-from-perfect measure, Dr. Yopp says. The test, CA19-9, measures proteins associated with pancreatic cancer, but the proteins also can be elevated when other conditions are present.

Science’s approach to classifying different cancers – and then treating them – is beginning to undergo a seismic shift, Dr. Yopp notes, from focusing on the physical location/organ site of a tumor to understanding the molecular pathways that drive unchecked cell growth. That reclassification will drive treatment decisions.

“Tissue banking and its subsequent research serve to eliminate a lot of these silos of one cancer versus another and looks at the disease as pathway-driven,” Dr. Yopp says. “That’s what the future is, chemotherapy based on mutational status and not just the cancer itself.”

**STEADY SUPPORT**

On their very first clinic visit, patients...
have a chance to connect with supportive services team members as well as volunteers from the local affiliate of the Pancreatic Cancer Action Network. Participants in the session learn how to access a full range of support professionals that can address needs related to their physical, emotional, spiritual, and financial health.

“All these pieces are really important to a patient’s journey,” Dr. Minter says. “But they’re often minimized, or attention is not paid to them until there’s a crisis and the patients need help, and they don’t know where to get it.”

Dietary support for pancreatic cancer patients at Simmons Cancer Center is comprehensive and proactive, introducing patients to concerns they should be aware of before they start treatment, while encouraging them to maintain food intake in order to support their recovery. Then, if any of a number of dietary problems arises, patients know how to get help right away, says clinical dietitian Shelli Hardy, M.C.N., RD, LD.

Common concerns after a Whipple procedure, for instance, include diabetes, malabsorption of fat (and fat-soluble vitamins), and slow emptying of the stomach. Malabsorption can often be treated with enzymes, but if the underlying cause is an overgrowth of bacteria in the small intestine, eating probiotic-rich foods such as yogurt and sauerkraut and minimizing snacking may be recommended.

Changes in appetite occur frequently regardless of what type of treatment the patient has received. In that case, patients are urged to eat small meals and make every bite count nutritionally (with guidance provided on how to increase protein and calories). Nutritional needs are likewise addressed for patients with nausea, who are counseled on how to take their anti-nausea medicines and on strategies to replenish fluids and electrolytes.

“I believe in letting people know that they shouldn’t tough anything out – nausea, poor appetite – because we’re here to help,” Ms. Hardy says. “And if you can tolerate your treatment, that’s your best shot at being successful.”

Music therapists are also available to pancreatic cancer patients at Simmons Cancer Center. Patients who are at the clinic when these professionals are present are likely to “hear us singing from the hallways,” says music therapist Christina Stock, M.A., MT-BC.

Ms. Stock introduces herself to patients and caregivers at the Support Session, and when she meets with them one-on-one, she assesses how they are managing the many stressors related to cancer and its treatment.
Music therapy addresses those concerns with calming music or a guided relaxation that can stabilize heart rates and increase oxygen saturation, she says. And learning a patient’s musical tastes, and what their cancer journey is like, can allow a therapist to write a new song, or rewrite lyrics of a familiar song, to fit the patient’s personal story and allow them to express themselves.

“Patients can benefit from music therapy if they’re experiencing anxiety, pain, depression, emotional or spiritual issues, family or caregiver stress, anxiety toward an upcoming medical procedure, or body image concerns,” Ms. Stock says.

Oncology social worker Catherine Credeur, LMSW, OSW-C, helps ensure patients and families can access all the services they require and are supported in their efforts to cope.

Individuals from outside the region may need to find financial support and lodging to receive care at UT Southwestern, or arrangements to be made for care and support to be provided in their hometown, by phone, or online. Patients and caregivers might benefit from guidance in understanding the Family and Medical Leave Act, extending employer health insurance coverage, or applying for disability benefits and later Medicare. Oncology social workers also consider how people are functioning at home and what community resources, such as home health/rehabilitation services, might be needed.

Mental health support is also crucial. “It’s part of my role as a social worker to assess where people are in their coping and if they can have their needs met with peer support and their care team, or if they need more formal mental health services – and then making the appropriate connections for them,” Ms. Credeur says. Cancer impacts not just each patient, but extended networks of family and friends, including in some cases young children, she says. As a social worker, she often assists with family concerns individually. Also, Simmons Cancer Center’s EMBRACE survivorship seminar series for patients, caregivers, and other loved ones addresses various family issues.

“Many people are surprised there is a family-centered focus here,” Ms. Credeur says. “Oncology social workers look at the patient as part of a family system that is all impacted by the cancer. We talk about how to explain cancer to the patient’s children or grandchildren, how to help teens and young adults express their thoughts, and how caregivers can sustain their health throughout their focus on the patient.”

PULLING IT ALL TOGETHER

Cancer centers across the U.S. have developed programs for pancreatic cancer patients. However, Simmons Cancer Center is among only a few that have assembled such comprehensive expert care at one site, with all of it centered on the patient experience.

“It’s one thing to get a couple of doctors in a room so they can huddle over a CT scan and call it a tumor board,” Dr. Beg says. “But to get all the supportive services together, standardize radiology reports, funnel the patients all through one channel for streamlined care – that’s really important.”

—Catherine Credeur
Oncology Social Worker
Innovations in pancreatic cancer prevention, care, and research at UT Southwestern are built on a foundation of excellence at Harold C. Simmons Comprehensive Cancer Center. Patients who seek cancer care at UT Southwestern benefit from:

**A FOUNDATION OF CARE**

Clemens University Hospital also has been identified as a Top Performer by The Joint Commission – a designation recognizing accredited hospitals that rate at 95 percent or above on numerous safety and quality accountability measures. According to U.S. News & World Report, Clemens University Hospital ranks in the top 4 in Texas, is designated as high-performing in cancer care, and is listed among the “Most Connected Hospitals” for 2015-2016, based on its commitment to the use of digital technology. UT Southwestern is also listed among Hospitals & Health Networks’ national “Most Wired” hospitals for a fifth consecutive year, thanks to its use of such technologies as databases to help physicians better identify high-risk patients and tools that keep physicians, nurses, and patients communicating effectively.

**EXTENSIVE DIGITAL INFRASTRUCTURE**

Patients’ electronic medical records encompass all care they have received at UT Southwestern, giving physicians instant access to information, imaging, and test results across hospitals, clinics, and disciplines. Patients themselves, along with designated family members and caregivers, may review test results or educational material, make and track appointments, request prescription renewals, print records for insurance or disability claims, and message their care providers as nonurgent needs arise through the University’s MyChart portal. MyChart is a popular computer tool for UT Southwestern cancer patients, research has shown, and is also accessible through an application for Android or iPhone platforms.

**TARRANT COUNTY CARE**

In Fort Worth, oncology care – including direct access to UT Southwestern’s pancreatic cancer surgical oncologists – is provided through the Moncrief Cancer Institute and a branch at Moncrief of Simmons Cancer Center. Oncology care at Moncrief features brand-new facilities, including exam rooms and private chemotherapy infusion rooms; secure telemicine consultation with specialists at UT Southwestern in Dallas; the latest imaging technologies; access to clinical trials; cancer genetic counseling and testing; on-site laboratory and specialty pharmacy services; and programs to promote health in cancer survivors, including nutritional counseling.

**AN URGENT CARE CLINIC**

For Simmons Cancer Center patients struggling with side effects of their cancer or treatment, the Urgent Care Clinic – open during business hours – is a backup clinic when regular providers are not immediately available. All calls are triaged to ensure patients in need of emergency care are sent to the emergency room. Outside normal business hours, patients may consult with a physician on call.

**THE CANCER ANSWER LINE**

Simmons Cancer Center’s free Cancer Answer Line (1-888-980-6050) addresses questions from community physicians, patients, family members, and others; offers education and resources; and can assist with patient referrals. The Cancer Answer Line fields almost 200 calls a month on topics such as cancer treatment and screening, clinical trials, quitting smoking, and more. Questions also are submitted through the Cancer Center’s website, at utswmedicine.org/cancer/community-outreach/cancer-info.html.
UT Southwestern’s William P. Clements Jr. University Hospital has two dozen advanced surgical suites and an entire floor, with 64 single-patient rooms, devoted to cancer care.
Simmons Cancer Center has joined forces with the nonprofit Pancreatic Cancer Action Network – a nationwide research, patient support, community engagement, and advocacy organization – to ensure at the outset of treatment that patients and their loved ones will be able to connect with any help they may need during the course of their cancer journey.

The two organizations worked side-by-side in developing the Patient/Family Support Session, a lunchtime meeting at which UT Southwestern professionals and the advocacy organization’s local affiliate volunteers offer education about the roles of patients’ medical and supportive care providers, along with guidance on how to navigate to a host of community resources. Typically during their first clinic visit, patients and family members attend the lunchtime session with UT Southwestern staff and the volunteers, while physicians in the Multidisciplinary Pancreatic Cancer Program meet to evaluate each case and determine treatment recommendations.

The Patient/Family Support Session was conceived to address the flood of information and emotions that can overwhelm patients and their caregivers after a diagnosis of pancreatic cancer, says volunteer Zach Weismann, a former Pancreatic Cancer Action Network Dallas-Fort Worth affiliate chair. “Cancer can feel very isolating; it can feel like you against the world,” he says. Session participants, who receive a printed packet of materials for reference, don’t need to understand all the resources at that moment, but just need to know they will be there when needed.

The learning curve can be fast and steep for patients, says Mr. Weismann, who lost his mother to pancreatic cancer in 2014. “For an average individual, dealing with cancer for the first time, you have this whole new vernacular,” he says. “I remember, with my mom, Googling ‘oncology’ and realizing there are multiple kinds of oncologists.”

The nonprofit’s resources address a host of concerns – for instance, the organization’s national Clinical Trial Finder can help patients find a study that might be appropriate for their medical and personal circumstances, if no such study is available at UT Southwestern. Patients also can be assigned a Patient Central Associate, available by phone and email, to provide personalized education and support.

“There is a lot of information available about pancreatic cancer, and it can be difficult for patients and their families to stay up-to-date,” says Kate Dishman, Manager of Patient Services Marketing at the Pancreatic Cancer Action Network. “This is why our free information and services are personalized – to ensure patients are empowered with the information they need to make the best treatment decisions. With the support of institutions such as UT Southwestern, we are able to reach more patients and provide these valuable resources.”

With a nationwide scope, the patient advocacy group’s resources can be especially helpful to a number of pancreatic cancer patients who seek care at UT Southwestern from out of town and who might not be able to regularly use the services the Cancer Center provides, says social worker UT Southwestern faculty and staff support community events to raise awareness, funds, and hope in the fight against pancreatic cancer.

COMMUNITY CONNECTIONS

A novel community partnership is helping to deliver a full range of support resources to UT Southwestern pancreatic cancer patients.
Catherine Credeur, LMSW, OSW-C.

The roles of the Pancreatic Cancer Action Network and UT Southwestern in the Patient/Family Support Session dovetail nicely, notes Mr. Weismann, adding that the program can serve as a model for other hospitals across the U.S. “It sounds so simple, just providing people (at a hospital) with our resources, but you’d be amazed at how infrequently it happens.”

The educational session also allows the Multidisciplinary Program’s supportive services team, which includes a social worker, dietitian, and music therapist, to reach out to patients. “A lot of people don’t really understand what social workers and dietitians do. Many people are not familiar with music therapy,” Ms. Credeur says. “We talk about how we are a complement to their potential treatment, how our disciplines weave into that to support their treatment and also focus not just on extending life, but the quality of life.”

The session helps the supportive services team build rapport with patients and families, making it easier for them to reach out when help is needed, says clinical dietitian Shelli Hardy, M.C.N., RD, LD. It also gives patients the tools they need to address possible symptoms proactively, before they arise or interfere with their treatment.

“You have to be proactive in this kind of setting,” Ms. Hardy says. “At other medical centers you often don’t see patients until they’re already having a problem, and it’s hard to work from a deficit, such as malabsorption (of nutrients) or a 10 percent weight loss.”

Patients and caregivers at the session also learn about assistance in many other areas, such as pain management, gastrointestinal side effects, and physical and occupational therapy. “All these pieces are really important to a patient’s journey and quality of life,” says Dr. Rebecca Minter, Director of the Pancreatic Cancer Multidisciplinary Program.

Knowing the tools available to assist them is vital to patients’ well-being before, during, and after treatment, she adds. “There are a lot of things patients actually have control over, at a time when they feel like they have no control.”

“There is a lot of information available about pancreatic cancer, and it can be difficult for patients and their families to stay up-to-date.”

—Kate Dishman
Pancreatic Cancer Action Network
PANCREATIC CANCER

RESEARCH’S PROMISE
Simmons Cancer Center is home to an array of groundbreaking pancreatic cancer research projects. Teams of scientists are developing and testing new treatments, identifying biological markers for detecting and monitoring pancreatic cancer, and elucidating molecular and developmental mechanisms that contribute to the disease.

**BENCH TO BEDSIDE**

Basic research begun more than a decade ago is coming to fruition in a promising new pancreatic cancer therapy, now being tested in clinical trials at UT Southwestern.

Foundational studies led by Dr. David Boothman, Simmons’ Associate Director of Translational Research, on the anti-cancer effects of a prodrug compound related to the natural substance beta-lapachone, has led to two collaborative, cross-disciplinary projects funded through the American Association for Cancer Research/Pancreatic Cancer Action Network.

The first project includes a multi-institution phase Ib clinical trial testing standard chemotherapy plus a formulation of beta-lapachone called ARQ761 (from the biotechnology firms NQ Oncology and ArQule). ARQ761 is aimed at providing the second of a one-two punch against pancreatic ductal adenocarcinoma (PDAC) after the chemotherapy, a combination of gemcitabine plus nab-paclitaxel (Abraxane), delivers the first blow by damaging the cancer’s DNA.

Dr. Muhammad Shaalan Beg, Assistant Professor of Internal Medicine and co-leader of the Cancer Center’s gastrointestinal disease-oriented team, is principal investigator for the trial at UT Southwestern. The trial represents the first time patients are being given ARQ761 in conjunction with chemotherapy.

In addition to years of laboratory research, the clinical trial is built on phase I safety testing conducted at UT Southwestern. That work, in various types of advanced solid tumors, has demonstrated that only patients with cancers testing positive for overexpression of the gene NQO1 – more than 80 percent of pancreatic tumors – appeared to benefit from ARQ761. NQO1 is also overexpressed in pancreatitis, a chronic inflammation of the pancreas that can increase risk of developing cancer.

The other project will explore the efficacy of combining ARQ761 with drugs known as PARP (poly [ADP-ribose] polymerase 1) inhibitors to treat PDAC, as well as other cancers in which NQO1 is overexpressed (Huang et al., Cancer Cell, 2016). A clinical trial of that combination is funded by the Simmons Cancer Center Developmental Therapeutics Grant and is expected to open in 2017, with Dr. Beg as principal investigator. (For the latest information about these and other clinical trials at Simmons Cancer Center, visit utswmedicine.org/cancer/clinical-trials)

The ARQ761-PARP inhibitor combination has proved effective against pancreatic, breast, and non-small cell lung cancer cells in a laboratory dish, and against human lung cancers implanted in mice. The trial is testing whether combining both types of drugs will allow relatively low doses of each drug, in order to minimize side effects.

**SEARCHING FOR SIGNPOSTS**

Dr. Thomas Wilkie, Associate Professor of Pharmacology, is applying his expertise in pancreas development and regulators of G-protein signaling (RGS) to several challenges posed by
pancreatic ductal adenocarcinoma (PDAC), the most common malignancy of the pancreas.

Dr. Wilkie and his colleagues, Dr. Yonghao Yu, Dr. Rolf Brekken, and Dr. Alan Schroit, are searching for biological signposts, or biomarkers, in blood that might give an early indication of pancreatic cancer in humans. These markers may indicate overactive signaling of KRAS or GNAS mutant genes, which can drive tumors to form. Specifically, the team is hoping to identify and develop biomarkers reflecting patterns of gene expression that occur in newly developing tumors and in fluid from pancreatic cysts, which can be precancerous.

Additionally, the Wilkie lab is pursuing biomarkers that could reveal when a cancer progresses after treatment. This could help scientists systematically test which new chemotherapies are effective. The team has shown that one such marker, Rgs16::GFP (a “transgene,” or a foreign gene transferred into mice), can serve as a signal for all stages of PDAC, gauging increasing tumor burden in KIC mice, which are genetically engineered to serve as models of human PDAC.

Further, using Rgs16::GFP, the researchers developed a preclinical model to efficiently screen drug combinations for pancreatic cancer that is driven by mutations in the KRAS gene. KRAS anomalies occur in the vast majority of human cases of PDAC and arise early in the course of the cancer. These mutations are also notoriously difficult for cancer drugs to neutralize.

In the KIC mice, the team administered a standard pancreatic cancer chemotherapy, gemcitabine plus nab-paclitaxel, for two weeks, plus
drugs to inhibit Axl, a receptor that is important for pancreatic cancer progression. By measuring levels of Rgs16::GFP, the team was able to rapidly discern the cancer’s response to the Axl-targeted therapy, compared with the response of mice receiving only gemcitabine with nab-paclitaxel, or just gemcitabine. The findings demonstrate that the approach could be used to identify effective medicines for pancreatic cancers, the researchers say.

Dr. Wilkie and his colleagues also are working to identify new PDAC antigens – substances that can train the immune system to attack the cancer.

FROM CYST TO CANCER

UT Southwestern surgical oncologist Dr. Sam Wang, Assistant Professor of Surgery, is exploring the role of the gene ARID1A in pancreatic mucinous cysts, which can be pre-cancerous.

Genomic studies have linked mutations in ARID1A, a putative tumor suppressor, to a broad array of malignancies, including cancers of the pancreas, breast, prostate, lung, brain, and ovaries. The gene is mutated in at least 10 percent of human pancreatic cancers.

Dr. Wang and his colleagues have been using a genetically engineered mouse model of pancreatic ductal adenocarcinoma to investigate the effects of ARID1A mutations. The mice carrying ARID1A mutations quickly develop large pancreatic lesions resembling human intraductal papillary mucinous neoplasms (IPMNs), which are benign cysts that can progress to invasive cancer.

The researchers are investigating how ARID1A mutations lead to cancer formation. “Since ARID1A itself is not druggable, we are trying to determine if ARID1A mutations activate pathways for which we have inhibitors,” Dr. Wang says.

A key goal is determining whether the timing of when ARID1A mutations are acquired affects the cancer. “We’re focusing on cyst formation right now, but in the future we want to determine if ARID1A mutations affect established cancers,” Dr. Wang says.

“This may determine if intervening on ARID1A-dependent pathways is feasible as a prophylactic strategy – that is, to prevent a benign cyst from transforming to a cancer – or it can also be used to treat patients who have already developed cancer.”

Other research involving Dr. Wang is beginning to evaluate levels of an enzyme called MMP7 as a possible preoperative indicator of which pancreatic ductal cancers – among those that imaging suggests are resectable – are likely to actually be metastatic and therefore unable to be controlled with surgery.

TRANSFORMATIVE STEPS

For more than a decade, Professor of Surgery Dr. Rolf Brekken, has been investigating pancreatic cancer, how its local environment affects tumor progression and treatment resistance, and how molecular signaling contributes to the ability of cancer cells to alter their cellular phenotype, a process known as plasticity.

In one line of research, he and his colleagues are studying the impact of collagen signaling on tumor progression. Collagen is abundant in pancreatic tumors and is involved in chemotherapy resistance and plasticity of epithelial cells, the cells of origin of pancreatic cancer. Receptors known as DDR1 and DDR2 are involved in collagen signaling; DDR1 in particular is plentiful on pancreatic cancer cells.

“It turns out this (signaling) pathway is important for tumor cell resistance to gemcitabine, a very relevant chemotherapy for pancreas cancer,” says Dr. Brekken, who with colleagues is performing preclinical testing on a DDR1 inhibitor known as 7rh and is pursuing commercial development of another novel inhibitor called TS101.

The work arose from earlier interest Dr. Brekken had in discovering the function of a protein called SPARC, which, as it turns out, inhibits collagen from binding to the DDRs. When SPARC is not present, DDR signaling is increased and tumors are much more aggressive, he says.

Dr. Brekken’s laboratory is also exploring whether immune therapy, which is showing great promise against some other cancers, can make a difference in pancreatic malignancies. “Right now immune therapy doesn’t work very well in pancreatic cancer, and the main question is, why?” he says.

A key strategy to answer that question uses an investigational antibody...
developed at UT Southwestern by the late Dr. Phil Thorpe, a professor of pharmacology, in whose lab Dr. Brekken earned his Ph.D. The antibody, bavituximab, is able to override the immune system's tolerance of a cancer, allowing patients to develop an antitumor immune response. Based on Dr. Brekken's studies in animals, it appears bavituximab reprograms the immune system so immune cells can recognize the cancer as dangerous – and may complement or synergize with immune-boosting cancer therapies such as nivolumab or pembrolizumab.

In other work, Dr. Brekken's group has found that the common blood-thinning drug warfarin can inhibit activation of Axl, a receptor expressed on pancreatic cancer cells, which is essential to epithelial plasticity and therefore important for tumor progression. The work was spearheaded by clinical trainees from the Departments of Surgery and Pediatric Hematology and Oncology in the Brekken lab who demonstrated that low-dose warfarin could prevent metastasis in preclinical models of pancreatic cancer by blocking Axl activation.

TRACING PDAC ORIGINS

Finding novel ways to conquer pancreatic ductal adenocarcinoma (PDAC) may rely on a clear understanding of where the cancer comes from in the first place. Although such tumors look like ductal tissue more than other types of tissue, another kind of epithelial cell, called acinar cells, might also give rise to the cancer, says Dr. Ray MacDonald, Professor of Molecular Biology. A mouse model of the disease, in which PDAC develops from acinar cells, provides a reliable picture of how the disease progresses in humans, he says.

“Something has to happen to the acinar cells,” he says. “If acinar cells lose their cellular identity, they convert to something that looks like a ductal cell. So we're investigating the nature of acinar cell identity, how losing their identity can bias them to be transformed into ductal-like carcinoma.”

For their studies, Dr. MacDonald and his colleagues generate a genetically engineered mouse line using a version of a human gene called KRAS that is mutated to promote cancer development. Such “oncogenic” KRAS mutations are present in more than 95 percent of human PDACs, Dr. MacDonald notes. In the mice, the researchers can induce expression of oncogenic KRAS just in the acinar cells of the pancreas.

“When we do that, we see precursors that are known in human pancreatic cancers,” he says, adding that those lesions appear in two or three months and then malignancies begin to show up in about a year. The lesions – microscopic precancerous anomalies called PanINs, or pancreatic intraepithelial neoplasia – are too tiny to be seen using current imaging technology and had been thought in human cancers to arise from ductal cells.

Dr. MacDonald believes the immediate surroundings of such a lesion probably drive cancer development. Inflammation of the pancreas – pancreatitis – is a strong predictor of human pancreatic cancer development, he says. And inducing pancreatitis in the human KRAS mice alters the identity of acinar cells and greatly increases the odds of tumor formation, affirming the potential role of acinar cells in the process.

“Inflammation disrupts the health of acinar cells. They turn off genes that characterize what they are; they normally make secretory enzymes in vast amounts, and the genes for those enzymes and other cell-identity genes shut off. And some genes that are characteristic of ductal cells of the pancreas or digestive cells of the stomach are turned on,” Dr. MacDonald says. “The disruption of the cells’ physiology and gene expression patterns makes them highly susceptible to transformation by oncogenic KRAS.”

But another molecular player apparently can limit the impact of KRAS. The research has identified a genetic enforcer for regulating acinar cell identity, a transcription factor gene called PTF1A. Inducing expression of oncogenic KRAS in virtually all the mice's pancreatic acinar cells yields only a relative handful of PanIN lesions, the scientists have found.

However, simultaneously inactivating PTF1A to disturb acinar cell identity yields many more lesions, which develop in just weeks instead of months.

Finding ways to maintain or re-establish acinar cell identity might lead to prevention of, or new therapies for, PDAC. “We think the acinar cell has a program, led by PTF1A, to maintain its identity, and part of that program resists the transformation by KRAS,” Dr. MacDonald says. In further work, the researchers are focusing on understanding acinar cells' metabolism, also influenced by PTF1A, as possibly a pivotal factor that allows the full destructive potential of KRAS to be unleashed.