Addressing Fertility Issues in Cancer Patients

By Joe Munch

For some newly diagnosed cancer patients, whether they will be able to have children after treatment is the furthest question from their minds—until the risks of therapy bring it front-and-center.

In recent years, improvements in treatment and survival expectations have increased the need for cancer patients to make informed decisions about addressing their risk of infertility following therapy.

“Back when the goal was to just have patients survive the disease, worries about whether they were going to be fertile definitely seemed to take a backseat,” said Dennis Hughes, M.D., Ph.D., an associate professor in the Division of Pediatrics at The University of Texas MD Anderson Cancer. “As we’ve gotten better and better at curing people, we’ve had to think more about what the rest of their lives will look like, and this includes their ability to have children.”

Assessing infertility risk

A patient’s risk of infertility depends on the specific treatment the patient will receive. Among chemotherapy drugs, for example, antimetabolites such as methotrexate carry a low risk of infertility, whereas alkylating agents such as cyclophosphamide carry a high risk. Radiation therapy is known to have a high risk of infertility, but methods such as radiation shielding and transposition—using surgery to temporarily move the ovaries out of the intended radiation field—are
used to mitigate that risk. Cancer surgery, unless it alters the reproductive organs, generally has a low risk of infertility.

The known risks of various therapies, and how those risks are handled, continue to change. For example, ifosfamide—a highly effective agent against sarcomas, which tend to strike adolescents and young adults—was once thought to have rendered them sterile but who—10, 15, 20 years later—appear to have recovered some fertility,” Dr. Hughes said. “Now I tell these guys, ‘You cannot count on the chemotherapy to be birth control for you, but when you want to have a child, you’re likely to have a great deal of difficulty having one that’s biologically your own.’”

The infertility risks of some newer therapies also remain unclear. For example, many targeted therapies inhibit enzymes, but all the actions of those enzymes are not always known.

“One of the misconceptions about targeted therapies is that they’re going to hit just their cancer targets. But some targeted therapies are going to hit multiple targets,” said Anna Franklin, M.D., an assistant professor in the Division of Pediatrics. “We know that these molecular targets are on the cancer, but they’re often in other places as well.”

In some cases, those other places are integral to fertility. For example, the ovaries of women receiving tyrosine kinase inhibitors such as imatinib do not respond to stimulation with hormone therapy; as it turns out, imatinib inhibits an enzyme critical to presenting the hormones to the ovaries.

**Discussing fertility**

Because decisions about fertility preservation must be made before treatment begins, discussions about the infertility risk posed by treatment tend to happen early.

“Typically, I bring up the risk of infertility in that first conversation about the diagnosis. Sometimes that’s not an easy conversation because people haven’t thought about it,” Dr. Franklin said. “And sometimes patients are so overwhelmed by their cancer diagnosis that they don’t hear about the risk of infertility.”

Noting that religious, cultural, and moral factors all may play into the decision, Dr. Franklin said, “It’s sort of a simple yes-or-no question—do you want to have children?—but it often leads to many other questions that must be answered.”

The conversation about infertility risk can be more difficult if the patient is a minor. Part of this difficulty stems from the awkwardness some parents and their children experience when discussing reproduction and sex, but it can also stem from differences in what parents and their children desire.

“Some 16-year-olds might have a very strong opinion about what they want their future to be like, but their parents are the medical decision makers,” Dr. Hughes said. “Sometimes, there’s a disparity between what the parents want for their child and what that adolescent wants for his or her future.” Regardless, he said, “The child really needs to assent to the therapy or the choice being made. The parents may decide, but the child in essence must agree to cooperate.”

To help address the fertility needs of its patients, MD Anderson recently hired Terri Woodard, M.D., an assistant professor in the Department of Gynecological Oncology and Reproductive Medicine. Dr. Woodard, a board-certified reproductive endocrinologist, splits her time between MD Anderson, where her role is purely consultative, and Baylor College of Medicine, where all procedural work—in vitro fertilization, oocyte cryopreservation, and even sperm banking—is performed.

“The beautiful thing about this partnership is that it offers patients streamlined access to an academic program with research support, great lab facilities, and a track record of doing well with infertility,” Dr. Woodard said.

“Some studies have shown that cancer-induced infertility can be as stressful as the cancer diagnosis itself.”

—Dr. Terri Woodard

At MD Anderson, Dr. Woodard talks to patients at all steps of their cancer journey, whether they have just been diagnosed and want to talk about strategies to preserve their fertility, are being treated for their disease and want to know what to expect later on, or are many years out from treatment and want to know about their fertility status. Most of her work centers on female cancer patients.

“All patients who are of child-bearing age are eligible for a consultation,” Dr. Woodard said. “Regardless of whether they have children already or how sick they are, patients really deserve to know what’s happening to them and what their risks are. If there is anything that could be done to preserve these patients’ fertility, they should have access to those options. Even some of the sickest patients tell us, ‘I know I’m not a candidate for doing this, but I’m glad you addressed that portion of me that always wanted to become a mother.’”

The first step in the consultation is to assess the person’s risk for infertility. To this end, Dr. Woodard often requests that patients undergo ultrasonography and blood tests to determine whether they are among the 15% of people in the general population who already have fertility issues. For these patients, she may advocate a more aggressive approach to fertility preservation.

After determining infertility risk, Dr. Woodard assesses the patient’s medical history and treatment plan to identify options for fertility preservation. The timing of the cancer treatments may dictate whether fertility preservation is possible.
Dr. Franklin said, “One of the issues we run into is that patients need to start treatment rather urgently. When you tell patients that you can preserve their fertility but will have to hold off on treating their cancer for several weeks, some of them will get very nervous.”

“Sometimes you just don’t have much of a choice,” Dr. Hughes said. “When a patient comes in and is already very ill, you may have to begin treatment as quickly as you can to fight back the malignancy, and there is not much time to address infertility risk.”

Finally, after discussing the risks and costs of each option as well as the time required to perform it, Dr. Woodard talks about what steps might be taken after treatment if patients choose to forgo fertility-sparing measures beforehand.

“Some people will come through cancer therapy and have normal fertility and get pregnant on their own the natural way; other people will need help; and other people will have permanent infertility,” Dr. Woodard said. For patients likely to have permanent infertility following cancer treatment, she will talk about options including adoption, using a gestational carrier, and using donor eggs or donor sperm. “I tell these patients that they might have to reframe how they think about becoming a parent, but if they want to be a parent, they still can be,” she added.

**Preserving fertility**

For men and postpubertal adolescent males, the approach to preserving fertility is relatively straightforward: these patients are referred to a sperm bank, where they provide a specimen that is subjected to semen analysis and infectious disease testing and then frozen and stored until they wish to have children. The longest time between banking sperm and using the specimen for successful in vitro fertilization is 25 years.

Not all males are able to easily provide viable sperm, however. In men who are unable to ejaculate—because of nerve damage from their cancer or its treatments, for example—electroejaculation may be used to procure a specimen. In males whose ejaculate does not contain sperm, testicular sperm extraction using fine-needle aspiration may be used.

Despite recent advances, harvesting a woman’s eggs remains a greater challenge, especially in cancer patients. For women and postpubertal females, the standard of care for fertility preservation now includes freezing the harvested eggs alone (oocyte cryopreservation) in addition to inseminating the harvested eggs and freezing the resultant embryos. Before any eggs can be harvested, however, the ovaries must first be stimulated with hormones to produce multiple eggs. This process takes 2–3 weeks, putting egg harvest and preservation beyond the reach of some patients who need to start treatment immediately.

One method that may provide an option for women who need immediate cancer treatment is ovarian tissue cryopreservation (OTC). In OTC, the part of the ovary that contains the eggs is surgically removed and frozen; after cancer treatment has ended, the tissue is thawed and reimplanted. Because OTC can be completed in a matter of hours, it can be used in patients who must start treatment immediately. In addition, because strong, estrogen level–elevating fertility medications are unnecessary with OTC, the procedure is theoretically a safer option in women with breast cancer or other hormone-sensitive cancers.

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**IN BRIEF**

**Intensity-Modulated Proton Therapy May Reduce Side Effects of Oropharyngeal Carcinoma Treatment**

The need for gastrostomy tubes for patients with oropharyngeal carcinoma decreases as much as 50% when patients are treated with intensity-modulated proton therapy (IMPT), according to a recent study conducted at The University of Texas MD Anderson Cancer Center.

The current standard radiation therapy for oropharyngeal carcinoma, intensity-modulated radiation therapy (IMRT), can damage surrounding delicate tissues. This damage can impair swallowing and cause patients to require gastrostomy tubes for adequate nutrition.

Conversely, IMPT allows for much more precise targeting of tumor tissues with less radiation delivered to the surrounding tissues. “IMPT is especially well suited for patients with the most complicated tumors of the head and neck, precisely painting the protons onto the tumor layer by layer,” said Steven Frank, M.D., an associate professor in the Department of Radiation Oncology and principal investigator on the study.

Dr. Frank’s group analyzed 25 patients treated with IMPT and 25 patients treated with IMRT and found that only 5 patients treated with IMPT required gastrostomy tubes, whereas 12 patients treated with IMRT required them. Similarly, the researchers found that patients treated with IMPT had a lower incidence of classic radiation therapy side effects, such as vomiting, nausea, and digestive tract inflammation.

The study’s results were presented at the American Society for Radiation Oncology’s 2013 annual meeting. Because of these promising results, Dr. Frank’s group has initiated a phase II/III clinical trial to compare the effectiveness and adverse event rates between IMRT and IMPT in patients with oropharyngeal carcinoma.

“With a recent epidemic of HPV-associated head and neck cancer among U.S. adults, there is a critical need to minimize the side effects associated with conventional IMRT that affect the patients’ courses of treatments—and ultimately the rest of their lives,” Dr. Frank said. “Since radiation therapy is the main tool to treat the disease in this fairly young group of patients, we must understand if more advanced technologies will provide additional value to them.”

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Fertility Issues in Cancer Patients

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However, OTC is extremely new and experimental; to date, only about 30 live births from women with reimplanted egg-containing ovarian tissue have been reported. Still, OTC is the only fertility-preserving option for prepubescent girls.

Similarly, testicular tissue cryopreservation, a fledgling technology in which spermatogonial stem cells are isolated from harvested testicular tissue, may one day enable prepubescent boys who require fertility-threatening cancer treatments to father children in adulthood. “The thought is that those stem cells can be matured outside the body and then be used for in vitro fertilization,” Dr. Franklin said. To date, however, no live births have resulted from using this technology.

For both OTC and testicular tissue cryopreservation, one concern is that removing tissue before treatment and reimplanting it after treatment has the potential to reintroduce the cancer. However, refining methods to screen the harvested tissues before reimplantation may address this concern.

“In girls with leukemia who had ovarian tissue harvested, researchers were able to do polymerase chain reaction tests for specific chromosomal translocations found in the patient’s leukemia cells. Finding those translocations in the ovarian tissue would be highly suggestive that there are leukemia cells in the ovaries,” Dr. Franklin said. “The same concern exists with spermatogonial stem cells. However, in boys with leukemia who had testicular tissue harvested, researchers were able to separate the spermatogonial stem cells from the leukemia cells through flow cytometry.”

**Monitoring fertility**

Just as important as addressing infertility risk before cancer treatment is monitoring fertility after therapy. Women who have undergone cancer treatments that would likely affect their ability to have children may experience menopause sooner than women who have not had such treatments. Therefore, closely following these patients for signs of early menopause and deciding whether to pursue egg harvest is essential.

The conversation about the effects of treatment on fertility bears repeating even after therapy has ended, Dr. Woodard said, because then patients who were overwhelmed with information and emotion at that initial discussion of their diagnosis may be more receptive to the information and more apt to remember it.

“[I] don’t think physicians always do a good job of communicating to patients that they should monitor their fertility after their cancer treatment,” Dr. Woodard said. “I’ve had quite a few patients who have come in on both extremes: some had no clue that they would have a fertility problem, and others assumed they couldn’t get pregnant because they had chemotherapy.”

In addition to revisiting the potential fertility issues stemming from treatment, Dr. Woodard recommends that 1 year after patients complete therapy, they undergo ultrasonography and blood tests to assess fertility. Decisions about future monitoring and potential treatments can then be made.

“We’re seeing these patients in our survivorship clinics and counseling them that we can check their fertility status and make decisions based on that,” Dr. Franklin said. “Do we need to think about harvesting some eggs now, or can we wait a few years? Or do we just need to monitor their fertility and assess it thoroughly when these patients are ready to have children?”

**“As we’ve gotten better and better at curing people, we’ve had to think more about what the rest of their lives will look like, and this includes their ability to have children.”**

– Dr. Dennis Hughes

**Battling cost**

The financial burden of preserving fertility after cancer treatment can be significant. For men who bank their sperm, the cost of the semen analysis, infectious disease testing, and 1 year of storage is around $650. For women who elect to freeze embryos or eggs, the cost is much higher, on the order of $15,000 per in vitro fertilization cycle.

“Women who are infertile for reasons other than cancer treatment may have been saving up for something like this. But cancer patients don’t necessarily think about fertility preservation, and then they need to do it fairly rapidly so they can start their cancer treatment. They don’t really have the option to plan for the expense,” Dr. Franklin said.

Some patients’ insurance plans cover these costs, but these tend to be the exception, not the norm—for now. The American Medical Association recently adopted a resolution stating that insurance should pay for fertility-preserving procedures. As in patients who require breast reconstruction following mastectomy, a treatment that causes infertility has resulted in a defect that has huge implications for the patient’s quality of life. With the increasing number of young cancer survivors, it may be only a matter of time before fertility-sparing treatments for these patients are covered by insurance.

“Some studies have shown that cancer-induced infertility can be as stressful as the cancer diagnosis itself and that the stress can persist many years after the patient has been cured. There can be a lot of regret in that, especially for people who had no idea that they might have had options to have their own biological children,” Dr. Woodard said. “As part of our informed consent process, we’re telling people that we’re giving them drugs or radiation that might cause these problems, and it’s our responsibility to offer solutions and make them available and acceptable for everyone.”

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Medical Advances Improve Bile Duct Cancer Treatment

By Jill Delsigne

Cholangiocarcinoma, the most common bile duct cancer, is a clinically silent disease in its early stages; patients usually present with advanced disease, which carries a poor prognosis.

In fact, patients with advanced cholangiocarcinoma have an average overall survival of only 1 year. But advances in diagnostics, radiation therapy, surgical resection, and targeted therapy are improving outcomes for patients with this disease.

Classification and staging

Cholangiocarcinomas are classified on the basis of their anatomical location: intrahepatic, perihilar, or extrahepatic. The importance of tumor location is reflected in the extensive changes to the staging of cholangiocarcinoma made in 2009, when the American Joint Committee on Cancer published the seventh edition of its cancer staging manual. Thomas Aloia, M.D., an associate professor in the Department of Surgical Oncology at The University of Texas MD Anderson Cancer Center, served on the committee that wrote these revisions. According to Dr. Aloia, “This new classification system recognizes the unique features of each tumor site instead of lumping all three categories together as one disease.” Correctly identifying the site of cholangiocarcinoma and accurately staging the cancer are crucial to determining the best possible treatment.

To enable physicians to more accurately diagnose and stage these tumors, Chusilp Charnsangavej, M.D., a professor in the Department of Diagnostic Radiology from 1983 to 2013, developed a computed tomography (CT) protocol for cholangiocarcinoma derived from a multiphasic thin-section pancreatic CT protocol. Dr. Charnsangavej’s innovations include the rapid injection of contrast material (4–5 mL per second for a total of 120–150 mL of contrast agent). The cholangiocarcinoma CT protocol results in much clearer CT images of the bile duct than was previously possible.

Standard treatment options

Therapy decisions for cholangiocarcinoma—most important, whether potentially curative surgery is possible—depend upon the size and location of the tumor, the presence or absence of metastases, and the patient’s general health.

The preferred initial treatment for cholangiocarcinoma has been surgery, when possible. However, only 10% of cholangiocarcinomas are surgically resectable.

Operable intrahepatic cholangiocarcinomas may require partial hepatectomy or hepatic lobectomy. To resect unilateral perihilar cholangiocarcinomas, surgeons may have to remove part of the liver, the involved bile duct, and the gallbladder. Perihilar cholangiocarcinomas with bilateral hepatic duct involvement may warrant a liver transplant. Occasionally, removal of a perihilar or extrahepatic cholangiocarcinoma requires a pancreaticoduodenectomy, also called a Whipple procedure.

If a cholangiocarcinoma cannot be completely removed, surgeons may bypass the blocked area and place stents to help keep the bile duct open. “One important cause of death in this disease is biliary sepsis that occurs secondary to obstruction of the bile duct and uncontrolled infection,” said Milind Javle, M.D., an associate professor in the Department of Gastrointestinal Medical Oncology. “Patients with this cancer are at risk of infections like cholangitis that need appropriate attention to biliary stent management and expertise in gastrointestinal endoscopy.”

Other treatments for cholangiocarcinoma include radiation therapy and chemotherapy. Unresectable cholangiocarcinoma may be treated with radiation, chemotherapy, or a combination of the two. For resectable tumors, chemotherapy and/or radiation can be used preoperatively to reduce the size of the tumor before surgery, but they are more often given as postoperative adjuvant therapy.

The most common chemotherapy regimen for cholangiocarcinoma is gem-
citabine with cisplatin or oxaliplatin; gemcitabine with capcitabine also is commonly used. For some patients, gemcitabine as a single agent is an appropriate choice of therapy. Regardless of the treatment modality, physicians must be careful not to damage too much healthy liver tissue, as patients need an adequate future liver remnant to survive.

Innovations in surgery
Cholangiocarcinomas with blood vessel involvement were previously considered unresectable, but advances in surgery have made potentially curative surgery possible in patients with such tumors. Surgeons can now perform extended liver resections that include the blood vessels because of advances in surgical techniques for blood vessel reconstruction.

A small group of patients with early-stage cholangiocarcinoma qualifies for liver transplantation. MD Anderson participates in a program in which such patients are selected according to a multimodality treatment protocol to undergo chemotherapy, radiation therapy, and surgical staging of their disease. After cancer treatment is done at MD Anderson, the patients are placed on a waiting list for a transplant, which is done at one of several transplant programs in the region. “Treating the cancer before liver transplantation is an important advance for patients who meet all the criteria,” Dr. Aloia said. He added that the program is currently focused on patients with early-stage cholangiocarcinoma because these patients do extremely well after the transplant.

Advances in radiation therapy
Advances in radiation therapy techniques in the past 5 years have allowed radiation oncologists to control for organ motion during treatment. These advances have greatly improved radiation treatment for intrahepatic cholangiocarcinoma. The radiation oncologists at MD Anderson use special CT protocols for cholangiocarcinoma to guide their treatment planning simulations to accurately target tumors.

Image-guided radiation therapy and proton therapy allow the delivery of high doses of radiation to cholangiocarcinomas while sparing nearby sensitive structures such as the stomach and intestine and preserving as much of the liver as possible. MD Anderson is one of the few institutions that have a CT scanner in the treatment room for imaging during the radiation procedure, allowing physicians to see organ movement and to identify where the radiation is deposited in real time.

Dr. Javle and Christopher Crane, M.D., a professor in the Department of Radiation Oncology, will be leading a recently approved phase III trial comparing chemotherapy followed by image-guided high-dose radiation therapy to chemotherapy alone in patients with unresectable cholangiocarcinoma. Dr. Crane said that the trial is based on results from a P01 grant–funded phase II study done in collaboration with Massachusetts General Hospital of image-guided proton therapy in a similar cohort of patients. “The majority of primary tumors were successfully controlled with a 3-week course of proton therapy,” Dr. Crane said. “We hope that the phase III trial will confirm these results.” This trial will include intensity-modulated radiation therapy and proton therapy as options and will begin enrolling patients at MD Anderson and other institutions soon.

Dr. Crane is hopeful about the new technique. “High-dose radiation for unresectable intrahepatic cholangiocarcinoma appears to have a dramatic survival benefit,” he said, “but this procedure must be done carefully.”

Drs. Crane and Aloia recently developed a new technique that allows radiation therapy for patients with unresectable cholangiocarcinoma near the stomach. Before, these patients could not receive radiation therapy because of the damage that would be done to the stomach. Using the new procedure, surgeons insert a spacer between the stomach and the liver to create enough distance (about an inch) to safely deliver high doses of radiation to the tumor.

Advances in targeted therapy
“Not only is cholangiocarcinoma diverse in terms of anatomical location, but it is also very diverse at the genetic level,” Dr. Javle said. “At MD Anderson, we are establishing a biliary cancer working group of clinical and research faculty and advocates who are committed to eradicating this cancer. The focus of our research is to assess any possible targeted therapy approaches.”

Much of the group’s research involves determining which genetic mutations are clinically relevant in cholangiocarcinoma. The KRAS gene, for example, is mutated in 30% of patients with cho-
Weight Loss Tips for Breast Cancer Survivors

Losing excess weight has multiple benefits

Most people assume that cancer treatment causes weight loss. However, many breast cancer survivors gain weight during and after cancer treatment.

During treatment, stress can lead patients to seek calorie-rich comfort foods and develop unhealthy eating habits that are later difficult to shake, leading to weight gain. These five tips are designed to help breast cancer survivors lose excess weight and keep it off.

Weight loss tips

**Eat and drink smart.** Suzanne Day, an advanced practice nurse in the Cancer Prevention Center at The University of Texas MD Anderson Cancer Center, recommends a diet high in fruits and vegetables. She also recommends that breast cancer survivors limit red meat and processed meats.

A special concern for breast cancer survivors is alcohol, which some studies have shown increases the risk of breast cancer recurrence. In addition to providing excess calories, alcohol may interfere with cell repair and the body's absorption of vitamins and minerals. Breast cancer survivors should limit their alcohol consumption to the standard recommendation of no more than one serving per day, although having fewer than three servings per week is even better. One serving equals 1.5 ounces of liquor, 5 ounces of wine, or 12 ounces of beer.

**Get moving.** Exercise not only burns calories but also increases muscle mass. Muscle burns more calories than fat, even at rest; so increased muscle mass helps keep weight off. For maximum benefits, exercise 30–60 minutes each day at an intensity that is enough for you to perspire. To avoid becoming bored with your exercise routine, consider exploring a wide range of activities. These can be anything from weight-bearing exercises to yoga.

Exercising may be difficult for some breast cancer survivors who have reduced mobility in the upper body after surgery. If you have reduced mobility, an exercise physiologist can identify appropriate activities that will help you ease into an exercise routine.

**Talk it out.** Studies have found that people who used support groups or counseling not only lost more weight but also kept off more of the lost weight. If in-person meetings aren't possible, online chat groups may help.

Another option is to say your goals out loud to yourself—hearing your goals spoken can help them seem more real. You can also discuss your goals with friends and family to get their support and stay motivated.

**Take it easy.** Some people may struggle to find the time to prepare healthy meals. Make things easier by buying healthy, pre-portioned foods. Healthy substitutions, such as a low-calorie protein bar instead of a candy bar, can make healthy eating easier.

Realistic exercise goals can also help you stay motivated and on track. Set daily and weekly goals that are achievable and then track your progress. Tracking your progress makes weight loss easier by helping you identify areas that need improvement.

**Change your thinking.** Clare McKindley, a registered dietitian in the Cancer Prevention Center, said, “Clients sometimes tell me that there is nothing new about nutrition that I can share with them with regard to weight loss. I help clients reflect on what has worked in the past and decide for themselves what it’s going to take to close the gap between knowledge and action.” Closing this gap between knowledge and action is essential for any weight loss plan.

One strategy for closing the gap between knowledge and action is to rethink your relationship with food. This can mean identifying “problem foods”—ones you eat too much of. Problem foods can be hard to resist when you’re bored, unhappy, or not feeling well. Plan ahead by having a healthy snack available and save those problem foods for when you’re feeling better. In a positive atmosphere, food cravings lose their intensity, so you’ll be less likely to overeat.

**Health benefits**

In addition to reducing risks for heart disease and diabetes, maintaining a healthy weight is important for breast cancer survivors because it reduces the risk of recurrence. While some risk factors for breast cancer, such as genetic mutations, are impossible to control, other factors can be controlled. Controllable factors like diet and exercise can decrease the risk of a first breast cancer or of recurrence in people who have had breast cancer before.

Fortunately, even small improvements in fitness can greatly improve health, and it’s easy to get started. Ms. Day’s advice for breast cancer survivors is short and sweet: “Drink less alcohol, exercise more.”

– M. Yeoman

**FOR MORE INFORMATION**

• Ask your physician
• Visit www.mdanderson.org
• Call the Cancer Prevention Center at 713-745-8040 or 800-438-6434
Bile Duct Cancer Treatment

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cholangiocarcinoma, and some targeted therapies are less effective in patients with mutations to this gene. Dr. Javle said that the majority of cholangiocarcinoma patients—those without KRAS mutations—could be candidates for cetuximab, erlotinib, or treatments that are directed against the epidermal growth factor receptor pathway. The results of early studies of such targeted therapies in patients with cholangiocarcinoma are promising.

Dr. Javle said testing for other oncogenes in cholangiocarcinomas can help guide therapy for patients with the disease. His group has found mutations in the ERBB2, BRAF, and FGFR genes as well as in genes responsible for chromatin modification, such as BAP1, ARID1A, and PBRM1. Finding genetic mutations might allow physicians to identify patients with subtypes of cholangiocarcinoma that can be treated with targeted therapies in addition to standard therapy.

Dr. Javle said, “If we can identify what diverse genetic types exist and then tailor therapy individually to those diverse types, we could alter the survival curve of this disease in the near future.”

MD Anderson has reached out to international research groups to continue exploring better treatment options for cholangiocarcinoma. Through the Global Academic Programs initiative, MD Anderson researchers and their international collaborators are investigating tissue banking, chemosensitivity studies, and molecular genetic profiling. Dr. Javle, for example, is collaborating with institutions in Chile and Thailand, and MD Anderson researchers have teamed with other international hospitals to develop collaborative strategies to combat cholangiocarcinoma.

Just as collaboration is essential in cholangiocarcinoma research, teamwork is key to treating patients with the disease. Dr. Javle said, “The treatment for this disease is complicated and in my view is best administered in a tertiary cancer center by an experienced multidisciplinary team. We need the services of experienced gastrointestinal endoscopists; we need experienced surgeons to operate; and innovative radiation techniques must be available for optimal management of this complex cancer.”

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FURTHER READING