

## Enhanced Surgical Recovery Programs Improve Perioperative Outcomes for Cancer Patients

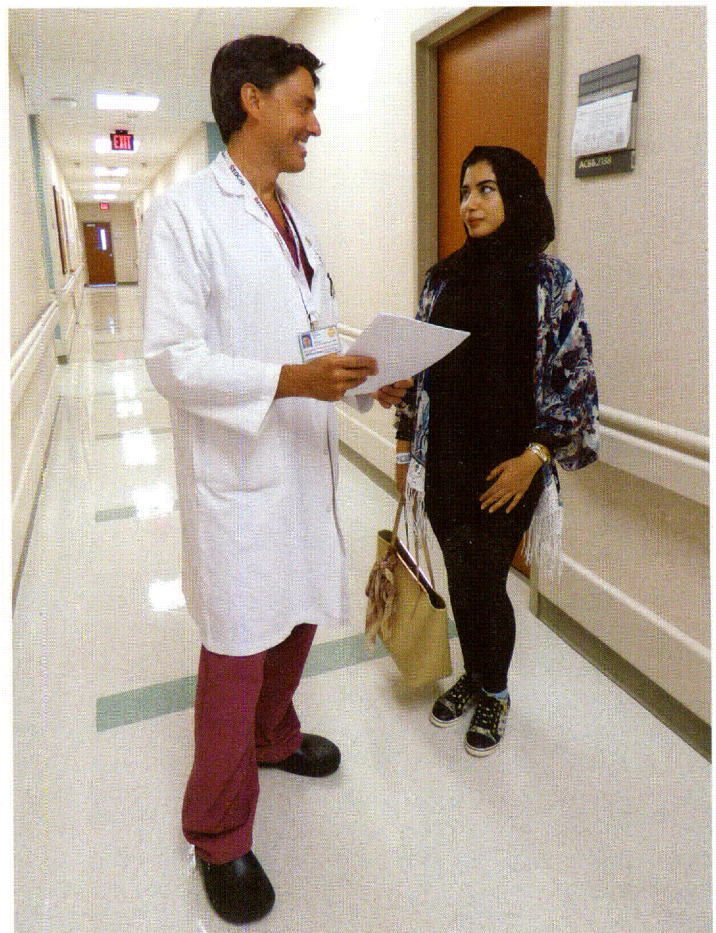
By Sarah Bronson

For patients undergoing cancer surgery, potential complications and long recovery times can delay the delivery of additional life-saving therapy. To improve patients' perioperative outcomes and clear the way for timely administration of additional therapies, several surgical teams at The University of Texas MD Anderson Cancer Center have begun using enhanced surgical recovery programs (ESRPs).

"After implementing ESRPs, we have seen reductions in symptom burden, improvements in functional recovery, reductions in length of stay, and fewer complications," said Vijaya Gottumukkala, M.D., a professor in the Department of Anesthesiology and Perioperative Medicine and an ESRP leader at MD Anderson. "These transformative results for our surgical patients stem from the collective efforts of our multidisciplinary teams."

### Principles of ESRPs

The ESRP approach combines various principles aimed at reducing morbidity from surgery. These principles include skipping routine preoperative bowel preparation, using mini-



*Dr. Pedro Ramirez and a patient discuss a treatment plan that includes elements of the enhanced surgical recovery program, an approach aimed at reducing patients' symptom burden and length of hospital stay while improving functional recovery.*

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## Enhanced Surgical Recovery Programs

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minimally invasive surgical techniques when possible, using goal-directed fluid therapy, minimizing the use of opioids in pain management, limiting the routine use of tubes and drains, and encouraging an early return to normal nutrition and physical activities, Dr. Gottumukkala said.

Where appropriate, ESRPs replace traditional practices with newer, evidence-based practices. For example, patients have traditionally been told not to eat or drink anything after midnight the night before surgery. But with the new approach, patients can drink clear liquids until 2 hours before arriving for surgery. This simple change means patients are better hydrated on the day of surgery. Likewise, ESRPs allow most patients to resume eating regular food on the same day of their operation.

At MD Anderson, ESRPs increasingly focus on the use of short-acting intravenous anesthetics instead of volatile anesthetic agents. These practices help minimize patients' postoperative confusion and allow them to emerge from anesthesia with less nausea, less vomiting, and better pain control, according to Dr. Gottumukkala.

Because each patient has unique needs, every patient may not receive each element of the ESRP approach. However, Thomas Aloia, M.D., an associate professor in the Department of Surgical Oncology and a co-leader of the ESRP for liver surgery, said that following the general principles and guidelines has resulted in noticeably better outcomes compared with the traditional approach.

### Incorporating the ESRP approach

Almost all patients are candidates for ESRPs, according to Pedro T. Ramirez, M.D., a professor in the Department of Gynecologic Oncology and Reproductive Medicine and a co-leader of the gynecologic oncology ESRP at MD Anderson. "One of our successes in the gynecologic ESRP is that we have been able to implement the approach in all patients undergoing open gynecologic surgery," he said. "And in December, we will initiate an ESRP for minimally invasive gynecologic surgery, so practically every patient who undergoes surgery in our department will receive an ESRP approach."

Implementing an ESRP can be challenging simply because its practices are nontraditional. Changing the approach requires commitment and cooperation across multiple disciplines, according to Javier Lasala, M.D., an assistant professor in the Department of Anesthesiology and Perioperative Medicine and a co-leader of the gynecologic oncology ESRP.

Dr. Ramirez agreed. He said, "The entire surgical team has to agree that ESRP is in principle a good thing for patients. There are so many points along the path where ESRP needs to be incorporated that if there is no unification in the surgical team, the patients are going to fall off that pathway. The surgeons, the anesthesia team, the nursing team, and others involved in patient care have to focus on making sure the patient receives the ESRP approach."

Dr. Gottumukkala also agreed,

emphasizing the contributions to ESRPs by clinicians from the divisions of Nursing and Pharmacy and the departments of Clinical Nutrition; Palliative, Rehabilitation, and Integrative Medicine; and Symptom Research.

At MD Anderson, the initial results of the first three ESRPs—in liver, gynecologic, and bladder surgery—have shown improvements in functional recovery and reductions in symptom burden as measured by the MD Anderson Symptom Inventory instrument, a patient-reported symptom severity scale. Since the initiation of the ESRPs, the median length of stay of patients who undergo open liver surgery has decreased by 2 days, and that of patients who undergo cystectomy has decreased by 3 days. In addition, total opioid consumption has decreased by up to 60% and opioid-related adverse events and gastrointestinal complications by up to 30%. These improvements are largely the results of the change in anesthetic strategies and a patient-centered multidisciplinary effort, according to Jay Shah, M.D., an assistant professor in the Department of Urology, and Juan Cata, M.D., an assistant professor in the Department of Anesthesiology and Perioperative Medicine. Drs. Shah and Cata co-lead the bladder surgery ESRP, which is also called the Optimized Surgical Journey.

The ESRP approach has the potential to influence long-term outcomes in patients. "By continuing this program and this approach," Dr. Gottumukkala said, "we aim to help patients return more quickly to their intended oncologic therapies, which ultimately may improve oncologic outcomes."

### Refining and expanding ESRP

Following the early success of the ESRPs in liver, gynecologic, and bladder surgeries, MD Anderson has initiated pilot programs for patients undergoing thoracic, colorectal, and spinal surgeries. And plans are under way to develop ESRPs for other treatments, in-

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**“We’re very encouraged to see the success of the program and the impact it’s having on patient care.”**

**– Dr. Pedro Ramirez**

cluding intracranial, head and neck, and reconstructive surgeries.

Furthermore, by capturing data that show which ESRP elements are used in which patients, MD Anderson clinicians seek to identify the elements most important to improving outcomes. “Our plan is to develop a system for prospectively collecting high-quality clinical data from patients. These data will include symptoms and functional interference at several time points, complications from surgery, length of hospital stay, readmissions, time to return to baseline functional status, and time to delivery of intended oncologic therapies,” said John Calhoun, a project consultant at MD Anderson’s Institute for Cancer Care Innovation.

Dr. Gottumukkala and the rest of the team expressed a hope that their data will lead other health care providers to see the value of the ESRP approach. “Increasing evidence is showing that there is absolutely a benefit to the patient,” Dr. Ramirez said. “It’s obvious which patients are in ESRPs—they have less pain, less nausea, and less vomiting; they’re eating sooner; and they’re getting back to daily activities sooner. We’re very encouraged to see the success of the program and the impact it’s having on patient care.” ■

#### FOR MORE INFORMATION

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Dr. Pedro Ramirez .....713-745-5498

## Prehabilitation

**M**any cancer patients undergo weeks or months of neoadjuvant chemotherapy before ablative surgery. Physicians have found that exercise regimens done during this preoperative period—prehabilitation—can help prepare patients for surgery and may even improve functional outcomes.

Like the ESRP approach, prehabilitation is aimed at improving functional outcomes and reducing surgical complications. But prehabilitation begins much earlier than do ESRP practices.

“The goals of prehabilitation before surgery are to improve patients’ functional status, reduce their postoperative complications, and ultimately enable them to receive additional cancer treatments,” said An Ngo-Huang, D.O., an assistant professor in the Department of Palliative, Rehabilitation, and Integrative Medicine. “Patients with poor performance status may not be able to receive certain treatments, but patients who are ambulatory, have better endurance, and have recovered well from surgery may be candidates for more aggressive therapies.”

Dr. Ngo-Huang provides prehabilitation guidance to patients who have a variety of cancers. Patients with spinal tumors may focus on strengthening their back muscles and other core muscles. Those with lung cancer may undergo intensive physical therapy and chest physiotherapy to improve their lung function and endurance. Patients with breast cancer may strengthen their arms and upper torso in anticipation of possible complications affecting the arms such as lymphedema or radiation fibrosis.

Each patient’s physical limitations also must be considered when planning the regimen. “In choosing exercises, we consider whether the patient has muscle loss, poor cardiopulmonary function, fatigue, a risk of fractures, or a risk of bleeding; and we consider the potential side effects of future treatments,” Dr. Ngo-Huang said.

From the limited evidence available so far, Dr. Ngo-Huang said, prehabilitation seems to lead to physiologic improvements that prepare patients for surgery and could contribute to better surgical outcomes.

For more information about prehabilitation for cancer patients, call Dr. An Ngo-Huang at 713-745-2327. ■



**Dr. An Ngo-Huang**

# New Treatments for Respiratory Viruses

By Bryan Tutt

**Viral respiratory infections are a major concern for immunocompromised patients, in whom such infections are difficult to treat and can lead to pneumonia and even death. Although few treatment options for such infections have been available, clinical trials of promising new therapies are now enrolling immunocompromised patients with two common respiratory viruses: respiratory syncytial virus (RSV) and parainfluenza virus (PIV).**

RSV and PIV infections start in the upper respiratory tract and can progress to the lungs. Especially vulnerable are leukemia patients and patients who have undergone hematopoietic stem cell transplantation, said Roy Chemaly, M.D., a professor in the Department of Infectious Diseases, Infection Control, and Employee Health at The University of Texas MD Anderson Cancer Center. “When these infections progress to pneumonia, immunocompromised patients are at high risk of dying,” he said.

“At MD Anderson, we see around 300 cases of upper or lower respiratory tract RSV infections each year, mostly between October and March,” Dr. Chemaly continued. “We see about as many cases of PIV, but most of these occur in the spring and summer.” Symptoms of RSV and PIV infections are similar to those of other respiratory viruses, and the differential diagnosis is made by polymerase chain reaction testing.

Once an RSV or PIV infection is diagnosed in an immunocompromised patient, its treatment can be a challenge. Little has changed in the treatment of RSV or PIV for the past 15 years, but Dr. Chemaly said research to improve treatment for both viruses is under way. He is the principal investigator of several clinical trials at MD Anderson that are currently enrolling

immunocompromised patients with RSV or PIV infections.

## RSV

The current treatment for RSV is aerosolized ribavirin, which is approved by the U.S. Food and Drug Administration (FDA) for treating RSV infections in children but is often prescribed off-label for immunocompromised adults. During this treatment, a patient must remain in a plastic tent at least 9 hours per day for 5–10 days. “This treatment works, but it is expensive and cumbersome,” Dr. Chemaly said. “So we are very excited about the possibility of treating RSV with an oral drug.”

In an MD Anderson–only phase II

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**“[I]n the past few years pharmaceutical companies have begun developing drugs that may improve outcomes for immunocompromised patients with RSV and PIV infections.”**

– Dr. Roy Chemaly

clinical trial, patients who have undergone hematopoietic stem cell transplantation and have RSV infections of the upper respiratory tract that require treatment are randomly assigned to receive aerosolized ribavirin or oral ribavirin. “This could change the way we treat patients, if we are able to move away from aerosolized ribavirin,” Dr. Chemaly said.

Another candidate for the treatment of RSV infection is GS-5806, a long-acting oral drug that blocks fusion of the viral envelope with host cells. The drug is under investigation in two multicenter randomized controlled trials for patients who have undergone hematopoietic stem cell transplantation and have RSV infections. One of the trials is for patients with infections of the upper respiratory tract; the other is for patients with lower respiratory tract infections.

In both GS-5806 trials, patients are randomly assigned to receive five doses of the drug or placebo over 17 days. The primary outcome measure for both trials is change in RSV nasal viral load; secondary measures include number of days without supplemental oxygen. For the trial enrolling patients with upper respiratory tract infections, Dr. Chemaly said, “We hope to prevent the virus from progressing to the lungs.”

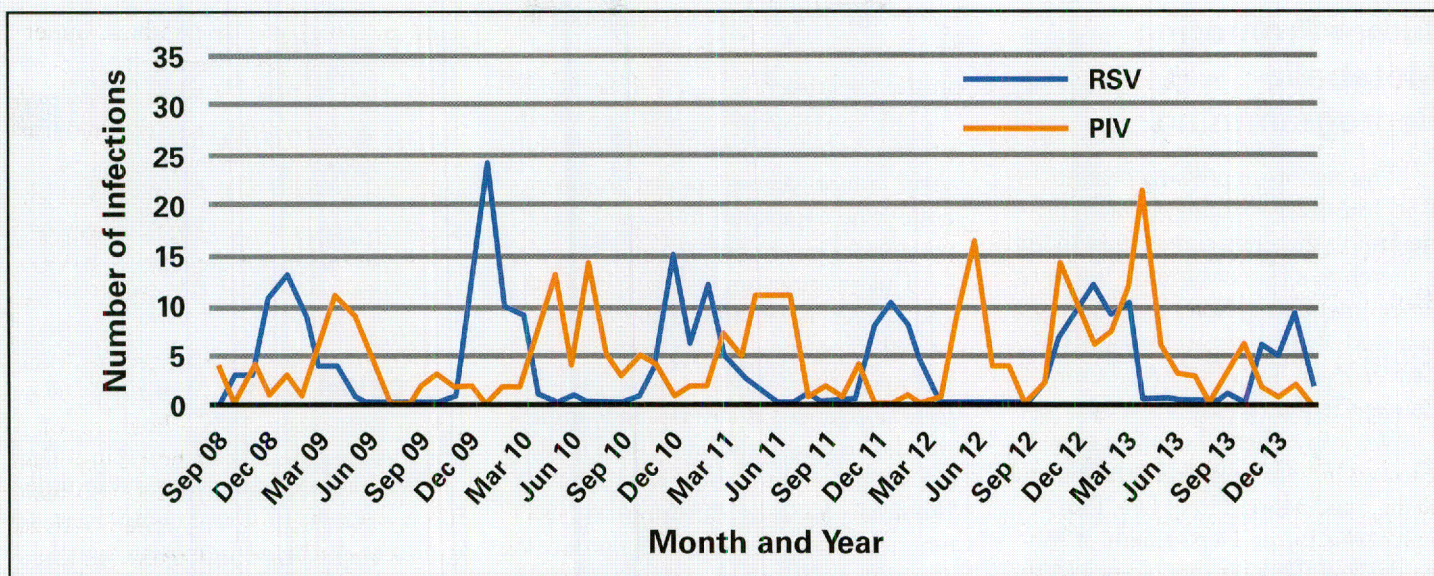
## PIV

Unlike RSV, PIV infection has no FDA-approved drugs for its treatment. “There’s nothing for patients with this infection, so there is a real unmet need,” Dr. Chemaly said.

Fortunately, an inhaled drug called DAS181 shows promise. DAS181 prevents the spread of PIV by blocking the virus from binding with sialic acid receptors in epithelial cells in the respiratory tract.

A multicenter phase II study of DAS181 is now enrolling patients who have undergone chemotherapy or stem cell, heart, or lung transplantation and have lower respiratory tract PIV infections necessitating supplemental oxygen.

# in Immunocompromised Patients



Respiratory syncytial virus (RSV) and parainfluenza virus (PIV) infections seen at MD Anderson in patients who have undergone hematopoietic stem cell transplantation.

Patients in the study are randomly assigned to receive one dose per day of DAS181 or placebo for 10 days. “Patients have a two in three chance of getting the study drug and a one in three chance of getting the placebo,” Dr. Chemaly said.

Interim results of the study are not yet available, but Dr. Chemaly is confident that the drug will benefit patients. “We have used DAS181 in our compassionate use program,” he said, referring to the FDA policy that allows expanded access to investigational drugs for individual patients when a clinical trial is not available, “and we’ve seen good results without many side effects.”

## Looking ahead

Dr. Chemaly is encouraged by the recent increase in new treatments for RSV and PIV infections. “For 10–15 years there was not much research on drug development for these viruses,” he said. “But in the past few years pharmaceutical companies have begun developing drugs that may improve outcomes for immunocompromised patients with RSV and PIV infections.” ■

## CLINICAL TRIALS: Respiratory Tract Infections

**An open label randomized controlled trial to prevent the progression of respiratory syncytial virus (RSV) upper respiratory tract infection to lower respiratory tract infection in patients after hematopoietic stem cell transplant (2011-0813).** Principal investigator (PI): Dr. Roy Chemaly. The purpose of the study is to learn if ribavirin can help to control RSV infection in patients with immune systems that have been weakened by stem cell transplantation and to compare the safety and effectiveness of the oral and inhaled versions of the drug.

**A phase IIB, randomized, double-blind, placebo-controlled multicenter study evaluating antiviral effects, pharmacokinetics, safety, and tolerability of GS-5806 in hematopoietic cell transplant recipients with RSV infection of the upper respiratory tract (2014-0717).** PI: Dr. Chemaly. The goal of this study is to learn if GS-5806 can help to prevent RSV from spreading to the lower respiratory tract.

**A phase IIB, randomized, double-blind, placebo-controlled multicenter study evaluating antiviral effects, pharmacokinetics, safety, and tolerability of GS-5806 in hematopoietic cell transplant recipients with RSV infection of the lower respiratory tract (2014-0718).** PI: Dr. Chemaly. The goal of this study is to learn if GS-5806 can help to prevent RSV from spreading in the body. Researchers also want to learn if GS-5806 can reduce symptoms caused by RSV infection.

**A phase II, randomized, double-blind, placebo-controlled study to examine the effects of DAS181 in immunocompromised subjects with lower respiratory tract parainfluenza infection on supplemental oxygen (2014-0385).** PI: Dr. Chemaly. The goal of this study is to learn if DAS181 can help to control parainfluenza virus infection in patients with weak immune systems. ■

## FOR MORE INFORMATION

Dr. Roy Chemaly .....713-745-1116

## FOR MORE INFORMATION

Visit [www.clinicaltrials.org](http://www.clinicaltrials.org).



## **14-3-3 $\sigma$ Protein Prevents Tumor-Promoting Metabolic Reprogramming**

The tumor-suppressing protein 14-3-3 $\sigma$  interferes with metabolic reprogramming that aids cancer growth and is therefore a potential target for anti-cancer metabolic therapy, according to a study led by researchers at The University of Texas MD Anderson Cancer Center.

“We know that all cancers grow by learning how to reprogram their metabolism,” said Mong-Hong Lee, Ph.D., a professor in the Department of Molecular and Cellular Oncology and the senior author of the study’s report. “Our study showed that 14-3-3 $\sigma$  opposes and reverses tumor-promoting metabolic programs.”

In breast cancer cell lines and in samples of tumor and normal breast tissues from breast cancer patients, Dr. Lee and colleagues found that 14-3-3 $\sigma$  regulated cellular energy metabolism, thus protecting healthy cells from metabolic reprogramming that supports tumorigenesis. By promoting the degradation of the proto-oncogene protein Myc, 14-3-3 $\sigma$  suppressed processes essential to this reprogramming, including glucose uptake, glycolysis, glutaminolysis, and mitochondrial biogenesis. The suppression of these processes by 14-3-3 $\sigma$  was demonstrated again in a mouse xenograft model.

Moreover, the loss of 14-3-3 $\sigma$  expression was found to result in tumor-promoting metabolic reprogramming.

*“14-3-3 $\sigma$  expression levels can help predict overall and recurrence-free survival, tumor glucose uptake, and metabolic gene expression in breast cancer patients.”*

– Dr. Mong-Hong Lee

And low levels of 14-3-3 $\sigma$  were associated with shorter survival durations in the patients whose samples were used in the experiments.

“14-3-3 $\sigma$  expression levels can help predict overall and recurrence-free survival, tumor glucose uptake, and metabolic gene expression in breast cancer patients,” Dr. Lee said.

This relationship between 14-3-3 $\sigma$  and cancer metabolism could be harnessed to prevent tumors from growing. Although the complex role of 14-3-3 $\sigma$  in tumorigenesis is still not fully understood, the study’s findings could guide the design of new cancer treatments. “Pharmacologically elevating 14-3-3 $\sigma$ ’s function in tumors could be a promising direction for targeted anticancer metabolism therapy development in the future,” Dr. Lee said.

This study’s report was published in *Nature Communications* in July. ■

## **miR-506 MicroRNA May Help Overcome Chemotherapy Resistance in Ovarian Cancer**

A noncoding RNA molecule that helps control gene expression may play a role in overcoming chemotherapy resistance among patients with the most common form of ovarian cancer, according to a study led by researchers at The University of Texas MD Anderson Cancer Center.

Epithelial ovarian cancer accounts for approximately 90% of all ovarian cancers. Most epithelial ovarian cancers, especially the high-grade serous subtype, tend to develop resistance to platinum-based chemotherapy drugs.

The researchers identified the microRNA miR-506 as a likely robust clinical marker for epithelial ovarian cancer patient survival and chemotherapy response and as a potential therapeutic agent owing to its ability to sensitize cancer cells to chemotherapy.

*“This study provides further insight into the role of miR-506 in augmenting chemotherapy responses by directly affecting the DNA repair process used by cancer cells.”*

– Dr. Wei Zhang

“We had previously found that miR-506 is a potent inhibitor of a process known as epithelial-to-mesenchymal transition, which is associated with chemotherapy resistance,” said Wei Zhang, Ph.D., a professor in the Department of Pathology and senior author of the study’s report.

Using data from The Cancer Genome Atlas and three independent data sets, Dr. Zhang and his colleagues found that high levels of miR-506 expression were associated with longer progression-free and overall survival in patients with epithelial ovarian cancer.

The researchers then performed in vitro and in vivo experiments to elucidate the role of miR-506 in chemotherapy response. In human high-grade serous epithelial ovarian cancer cells, miR-506 directly targeted the double-strand DNA damage repair gene *RAD51*, sensitizing the cells to damage from platinum-based chemotherapy drugs. In a mouse model of high-grade serous epithelial ovarian cancer, the addition of miR-506-loaded nanoliposomes to platinum-based chemotherapy significantly improved treatment responses.

“This study provides further insight into the role of miR-506 in augmenting chemotherapy responses by directly affecting the DNA repair process used by cancer cells to counter DNA damage caused by chemotherapy,” Dr. Zhang said.

The results of the study were published in the July issue of the *Journal of the National Cancer Institute*. ■



# Types of Drugs Used to Treat Cancer

## Cytotoxic, targeted, and immunotherapy drugs have different functions and side effects

**When we think about cancer-fighting drugs, “chemotherapy” may be the first word that comes to mind.** But this word covers a wide range of anticancer drugs that vary in their actions and side effects. Understanding the different types of anticancer drugs is helpful for patients and their families and friends.

Most anticancer drugs belong to one of three general types: cytotoxic, targeted, or immunotherapy. Cytotoxic drugs kill all types of cells since the drugs cannot distinguish cancer cells from healthy cells. This group includes most traditional chemotherapy drugs. Targeted agents, a newer type, interact with and disrupt the activity of specific molecules that promote the growth of cancer cells. Immunotherapy drugs stimulate the body’s immune system to fight cancer.

For patients, the main difference in the types of drugs is their side effects. Because cytotoxic drugs affect all the cells in the body, these drugs may have severe side effects. Not all cytotoxic drugs cause the same side effects, but hair loss, nausea, and fatigue are common side effects of some of these drugs. Some cytotoxic drugs can cause nerve damage. Others cause difficulty with concentration and memory. In contrast, targeted drugs affect mostly cancer cells and tend to have less severe side effects, which may include fever, diarrhea, problems with blood clotting and wound healing, skin problems, high blood pressure, or liver problems. And some immunotherapies may cause flu-like symptoms, rashes, or a drop in blood pressure.

### Cytotoxic therapies

Cytotoxic drugs kill cancer cells or damage them so that they cannot replicate (divide into two copies). Cytotoxic agents are categorized according to their function, structure, and relationship with other therapies. It is important to note that some drugs can be classified in more than one of the groups below.

- *Alkylating agents* damage cells’ DNA

so that the cells cannot replicate.

- *Antimetabolites* substitute for the building blocks of RNA or DNA and interfere with RNA or DNA replication.
- *Antitumor antibiotics* attack the DNA of cancer cells so that the cells cannot continue to grow and replicate.
- *Topoisomerase inhibitors* disrupt the activities of enzymes (a type of protein) that aid in the separation of DNA strands during DNA replication.
- *Mitotic inhibitors* stop mitosis, a process where a cell splits into two daughter cells.

### Targeted therapies

Targeted therapies, also known as molecularly targeted agents or precision medicines, are designed to block the actions of a specific target—usually a protein or gene that is directly or indirectly involved in the growth and progression of cancer. There are two main forms of targeted therapies, small-molecule drugs and monoclonal antibodies, and each form targets cancer cells in a different way.

Small-molecule drugs have the ability to enter cells and interact with target proteins within the cells. Many small-molecule drugs have generic names that end in *-ib*.

Monoclonal antibody drugs function like natural antibodies, which are proteins that bind to target proteins on the surfaces of bacteria, viruses, or cancer cells so that the body’s immune system can locate and destroy the invading cells. Monoclonal antibody drugs have generic names that end in *-mab*.

Targeted drugs can also be sorted into different types according to their function. As cancer research progresses, the number of types increases. A few common types of targeted drugs are listed below.

- *Signal transduction inhibitors* block enzymes that signal cancer cells to replicate.
- *Apoptosis inducers* cause controlled

cell death in cancer cells.

- *Angiogenesis inhibitors* block the formation of new blood vessels to tumors.
- *Hormone therapies* stop the body from making hormones that certain types of cancer need to survive. Although these drugs work against a particular hormone, most do not target a specific molecule the way small-molecule drugs and monoclonal antibodies do.
- *Antibody-drug conjugates* are drugs in which a molecule of a cytotoxic drug or radioactive agent is linked to a monoclonal antibody that targets cancer cells.

### Immunotherapies

Immunotherapies help the body’s natural immune system fight cancer. Some targeted drugs, such as monoclonal antibodies, are also considered immunotherapy drugs because they stimulate an immune response against a specific protein. Other immunotherapies stimulate a general response by the immune system. Two common types of these nonspecific immunotherapies are listed below.

- *Interferons* boost the ability of the body’s immune cells to fight cancer or infections.
- *Interleukins* help immune cells grow and replicate more quickly.

### Treatment combinations

Cytotoxic, targeted, and immunotherapy drugs can be used with each other and other forms of cancer treatment, such as surgery and radiation therapy. Since cancer cells can develop a resistance to cytotoxic or targeted therapies, such combinations of treatments are often recommended. ■

—K. Nair

### FOR MORE INFORMATION

- Ask your physician
- Visit [www.mdanderson.org](http://www.mdanderson.org)
- Call askMDAnderson at 877-632-6789

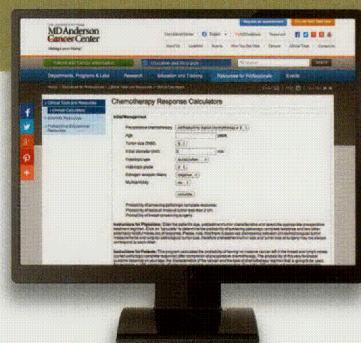
## USEFUL RESOURCES

### Clinical Calculators

Cancer treatment decisions must be made with consideration of multiple patient and disease characteristics. To help physicians make evidence-based treatment recommendations, experts at The University of Texas MD Anderson Cancer Center have developed a series of online clinical calculators.

The clinical calculators, or nomograms, are designed to predict survival or treatment outcomes for patients with various cancer types. The clinical calculators make these predictions on the basis of patient data entered by the physician. For example, the calculator for predicting response to neoadjuvant chemotherapy for breast cancer prompts physicians to enter the patient's age; the neoadjuvant chemotherapy regimen; the tumor's T category, diameter, histologic type and grade, and estrogen receptor status; and whether the tumor is multicentric. From this information, the calculator predicts the patient's probability of achieving a pathological complete response to neoadjuvant chemotherapy, of having a residual invasive tumor less than 3 cm in diameter after neoadjuvant chemotherapy, and of being a candidate for breast-conserving surgery.

Other clinical calculators for breast



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cancer treatment predict disease-free survival after breast surgery; residual cancer burden; lymph node status with or without neoadjuvant chemotherapy; and—for women 66–79 years old—the likelihood of benefiting from radiation therapy after breast-conserving surgery. Clinical calculators are also available to predict lymph node involvement in patients with esophageal cancer and survival outcomes for patients with cancers of the colon, rectum, or pancreas.

The clinical calculators were developed using data from peer-reviewed journal articles to be used in conjunction with medical opinions by qualified physicians.

The clinical calculators are available at [www.mdanderson.org/education-and-research/resources-for-professionals/clinical-tools-and-resources/clinical-calculators/index.html](http://www.mdanderson.org/education-and-research/resources-for-professionals/clinical-tools-and-resources/clinical-calculators/index.html). ■

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