

REPORT TO PHYSICIANS

JULY 2010 VOL. 55, NO. 7

# Oncology

## Refining Approaches to Thyroid Cancer

Time-proven treatments and newer biologic agents offer hope, particularly for patients with advanced disease.

By Joe Munch

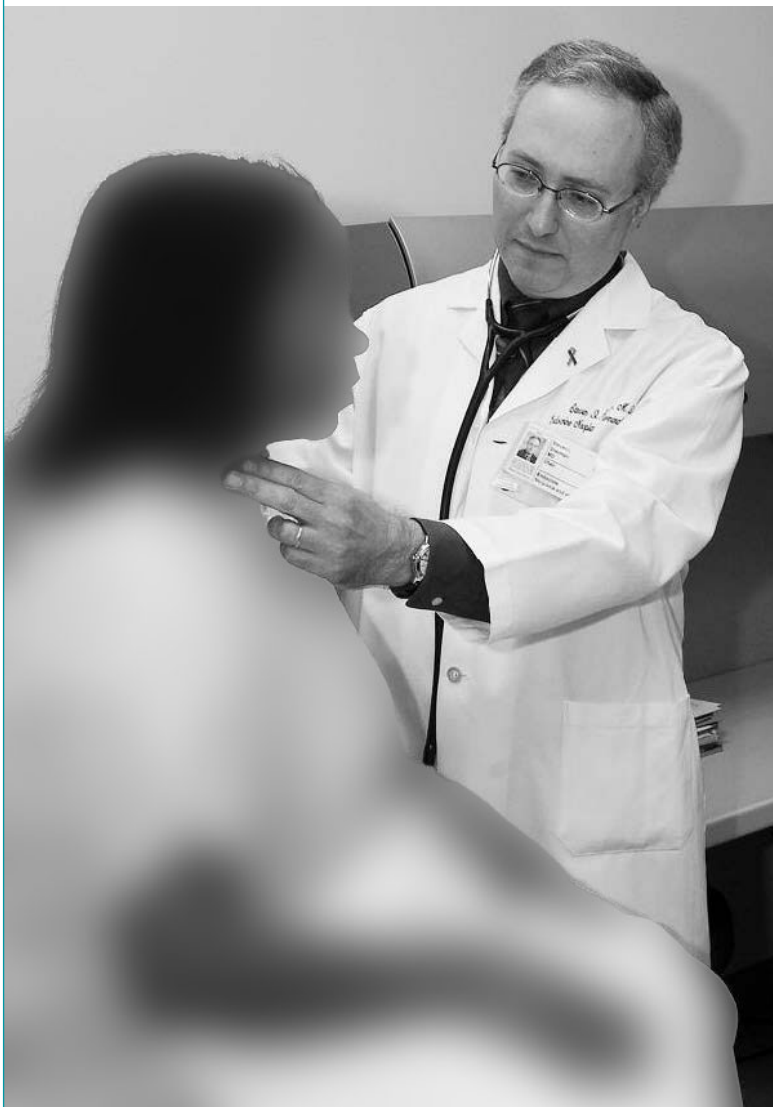
**A**lthough the well-established therapies for thyroid cancer have proven effective in the vast majority of patients, they sometimes fall short in patients with progressive disease. However, recent advances in surgical techniques, paired with a burgeoning pool of potential targeted therapies, are changing this therapeutic landscape for thyroid cancer.

“Patients with advanced thyroid cancer now come to us with an expectation—not necessarily an expectation that they’ll be cured, but an expectation that there is something possible, that there may be a treatment that can help, that there could be a clinical trial they can participate in,” said Steven I. Sherman, M.D., a professor in and chair of The University of Texas MD Anderson Cancer Center’s Department of Endocrine Neoplasia and Hormonal Disorders. “They have hope simply knowing now that there’s active ongoing research, which 5 years ago did not exist. Our biggest obligation is to fulfill that hope.”

*(Continued on page 2)*

**Dr. Steven I. Sherman**  
(right) says recent research has offered new hope to patients with advanced thyroid cancer.

THE UNIVERSITY OF TEXAS  
**MD Anderson  
Cancer Center**



## Refining Approaches to Thyroid Cancer

(Continued from page 1)

### Surgery

When oncologists talk of thyroid cancer, they almost invariably mean papillary or follicular (differentiated) thyroid cancers, which together account for approximately 90% of all thyroid cancers. (Other types of thyroid cancer include medullary thyroid cancer, which accounts for 5%–10% of thyroid cancers, and anaplastic thyroid cancer, the rarest and by far the most aggressive thyroid cancer.) The first-line treatment of papillary and follicular thyroid cancers has, at least since the 1950s, been surgery: partial or total thyroidectomy and, if indicated by ultrasonography-guided fine-needle aspiration cytology, lymphadenectomy. And there is little evidence to suggest that this will change any time soon.

“Surgery is going to remain the mainstay of frontline treatment for thyroid malignancies for the foreseeable future because it’s so effective,” said Gary Clayman, M.D., a professor in MD Anderson’s Department of Head and Neck Surgery. “In many patients, thyroid cancer tends to be a very localized, relatively slow-growing malignancy. Many times it is surgically curable with exquisitely low morbidity.”

According to Dr. Clayman, the success of surgery for thyroid cancer depends heavily on thoroughly evaluating the patient prior to surgery to acquire as accurate a diagnosis as possible. This assessment includes an analysis of thyroid function and comprehensive ultrasonography of the thyroid bed, neck, and superior mediastinum to determine the extent of local disease and lymph node involvement. When appropriate, cross-sectional imaging with computed tomography can help define the complete tumor extent to optimize surgical planning.

“It’s really best for patients to have the right surgery as their first surgery if at all possible. Prospective clinical trials have shown that some 11% of patients have incomplete surgery as their first surgery. In these patients, the mass may have been pathologically misinterpreted or the extent of disease was not anticipated or appreciated preoperatively,” Dr. Clayman said.

Even when the extent of the disease is known, the surgery itself can be chal-

lenging. The thyroid gland is adjacent to the larynx, the trachea, the esophagus, the superior and recurrent laryngeal nerves, and a number of miniscule muscles that are essential to swallowing—not to mention the parathyroid glands, which control calcium homeostasis and use the same blood supply as the thyroid gland. Identifying and preserving these structures while removing all evidence of disease is crucial to reducing patient morbidity.

Traditional open thyroidectomy is performed through a 3–5-cm incision in the neck. However, minimally invasive video-assisted thyroidectomy and robotic thyroidectomy, which allow surgeons to access the thyroid area through smaller or less obvious incisions, are being used with increasing frequency. Although each method has certain advantages over traditional open thyroidectomy and is appropriate for use in specific patients, Dr. Clayman believes that neither approach is sufficiently developed to be used in many patients, including those with known metastatic disease in the cervical region.

“I think that advances in some of the instrumentation are forthcoming and will usher in greater capabilities. Right now, I think we’re in an investigation or learning curve, particularly for robotic surgery,” Dr. Clayman said. “There will be continued refinements in thyroid surgery. I believe that automation and robotics instrumentation will continue to advance and take us to higher, more refined levels of patient care, evaluation, surveillance, and management.”

### Adjuvant treatments

Following surgery for thyroid cancer, most patients receive thyroid hormone therapy, not only to compensate for the function of the resected thyroid gland but also to prevent recurrent disease.

“Intuitively, patients receive thyroid hormone because they no longer have a thyroid,” Dr. Sherman said. “But as our data have shown, giving patients a little more thyroid hormone than what their bodies need improves survival following surgery.”

Most patients with nonmetastatic differentiated thyroid cancer also receive radioiodine therapy, an adjuvant treatment

that has been used for more than half a century. Patients are given iodine-131, a radioisotope that is taken up exclusively by normal and malignant thyroid cells and that emits beta radiation to kill the cells. However, malignant thyroid cells can lose their ability to take up iodine, rendering radioiodine treatment ineffective and allowing the disease to progress.

“In selected patients with metastatic disease, radioiodine can be helpful. But for a great many patients—perhaps the majority of patients—with metastatic thyroid cancer, radioiodine doesn’t do any good,” Dr. Sherman said.

Other thyroid cancer patients with metastatic disease—particularly patients with metastases in the brain and bone—may benefit from external-beam radiation therapy. External-beam radiation therapy is also indicated in a small subgroup of patients who have undergone surgery for papillary thyroid cancer; these patients typically are older than 40 years and have deeply invasive cancers involving the trachea, larynx, or esophagus or recurrent disease in one of these areas that cannot be effectively resected with a second operation. However, external-beam radiation therapy is used sparingly because of its potential side effects, including an increased risk of second cancers.

In the rarest of cases, patients with progressive disease and for whom radioiodine therapy and external beam radiation have failed will receive adjuvant cytotoxic chemotherapy.

“Chemotherapy, whether with doxorubicin or other agents, has historically been a salvage type of effort in thyroid cancer patients,” Dr. Sherman said. “Most patients who die from thyroid cancer never received chemotherapy.”

### New and experimental treatments

Historically, Dr. Sherman said, thyroid cancer patients were not enrolled in phase I trials (let alone phase II or III trials) in part because the trials were considered last-ditch salvage opportunities and because most thyroid cancers progress fairly slowly. But the discovery of the roles of oncogenic mutations and angiogenesis in thyroid cancer helped open the doors to clinical trials for patients with thyroid cancer that progresses despite standard treatment.

# Thyroid Cancer in Children

By Joe Munch

Adult and pediatric thyroid cancer patients receive essentially the same treatments. However, the contexts in which these treatments are given, as well as their outcomes, vary greatly.

“Children are often treated as we treat adults because there hasn’t been a lot of focused research on pediatric thyroid cancer,” said Steven Waguespack, M.D., an associate professor in and deputy chair of MD Anderson’s Department of Endocrine Neoplasia and Hormonal Disorders. “Thyroid cancer is rare in children younger than 10 years. There might be one case diagnosed per million children per year, if that.” Papillary carcinoma accounts for about 90% of pediatric thyroid cancers.

Children, particularly those younger than 10 years, tend to present with more extensive disease than adults: more than 80% of pediatric thyroid cancer patients have lymph node metastases, and 10%–20% have lung metastases. However, prognosis is excellent for most of these patients, with long-term survival the norm.

“It’s a paradox that children with papillary thyroid cancer typically present with an advanced extent of disease, yet their prognosis is excellent,” Dr. Waguespack said. “If a 50-year-old man presented with lung metastases

from thyroid cancer, his 5-year survival chances would probably be 50% or less, whereas a child can present with diffuse lung metastases and have a 5-year survival of 100%. So one of the concerns we have in treating children is that we want to treat their cancer effectively during childhood without harming them 20, 30, or 40 years down the road.”

Several factors may account for the excellent prognosis for children with thyroid cancer. Children’s thyroid tumors may be more sensitive to the effects of thyroid stimulating hormone suppression, or the disease may be especially iodine-avid. Genetic mutational status may also contribute to longer survival and better response. Whereas adults with papillary thyroid cancer often have a *BRAF* mutation in the tumor, which may be associated with tumor recurrence and decreased iodine avidity,



Dr. Steven Waguespack

this is not the case in pediatric patients, who tend to have a *RET/PTC* rearrangement as the inciting genetic event, particularly in radiation-induced tumors.

The most important initial step in treating any patient with thyroid cancer is to clear the neck of malignancy via surgery, which includes thyroid resection and lymph node dissection. Surgery is essentially the same for children as it is for adults, and it is best performed by a highly experienced surgeon. After surgery, the child is assessed for residual and metastatic disease that could potentially be treated with radioactive iodine. The child’s age, pathologic findings, clinical presentation, and extent of metastatic disease determine whether

radioiodine is given and, if so, how much is administered. Some patients may require multiple doses of radioiodine after surgery.

“One big question is, how long does one wait after the initial dose of radioiodine before giving another dose?” Dr. Waguespack said. “I wait at least a year, not 6 months as some guidelines say, because I would like to minimize the amount of radiation exposure in a child who has a malignancy that is typically not life-threatening and also because it can take 1 or more years to see the full effect of the first dose of radioactive iodine.”

However, Dr. Waguespack said, not all children need radioiodine therapy. “It used to be a knee-jerk reaction—surgery would be followed by radioactive iodine, no questions asked. But now radioiodine is given on more of a case-by-case basis. There are some children I am not treating with radioiodine because the risks of treatment outweigh the benefits,” Dr. Waguespack said. “You’re basically giving a dose of radiation to a child who has a lot of life ahead of him or her, and when you give that child radiation, you potentially place him or her at risk for secondary tumors decades in the future.”

In the exceedingly rare case of life-threatening thyroid cancer in children, targeted agents may be considered. Sorafenib, an oral multikinase inhibitor that was found to have activity against papillary thyroid cancer in phase II clinical trials in adults, has been used to treat several children with progressive, non-iodine-avid papillary thyroid cancer. ●

For more information, contact Dr. Waguespack at 713-792-2841.

“We recognized that, in general, a lot of phase II clinical trials arise because of early signals suggesting drug activity or benefit in phase I trials,” Dr. Sherman said. “With the emergence of drugs like tyrosine kinase inhibitors and biological findings suggesting that some of these drugs might have a benefit in thyroid cancer, we took the approach that, in the absence of a standard effec-

tive treatment for patients with progressing disease, it was perfectly ethical and appropriate to put such patients into phase I trials.”

As a direct outgrowth of the phase I trials, two investigational drugs—motesanib and E7080—moved into phase II studies for thyroid cancer. A third investigational drug, XL184, was so successful in a subset of thyroid cancer patients

that it went directly to an international randomized phase III trial.

“The overwhelming majority of patients who go into these studies and respond to the treatment being studied have a partial response, or their cancer stabilizes and may remain stabilized for years,” Dr. Sherman said. “Some patients have been on these drugs continuously

(Continued on page 8)

# Locoregional Cancer of the Esophagus

## Timing Surgery and Other Therapies for Resectable Disease

By Sunni Hosemann

### Introduction

More than 90% of esophageal cancers are either squamous cell carcinomas or adenocarcinomas. This discussion focuses on those two types of esophageal cancer, specifically the intermediate stages known as locoregional disease.

Locoregional disease is defined here as resectable disease that has invaded beyond the submucosa and may involve regional lymph nodes and other structures including the pleura, pericardium, or diaphragm. Locoregional disease is thus differentiated from early disease (a tumor that is in situ or involves only the lamina propria or mucosal layers of esophageal tissue) and from disease that is unresectable or has metastasized beyond the regional lymph nodes (having spread to distant lymph nodes, distant organs, or certain adjacent structures, such as the aorta, vertebral body, or trachea).

Several treatment approaches for locoregional disease are currently considered standard, but for individual patients, there are options that require considerable analysis and discussion.

### About Esophageal Cancer

Esophageal cancer is not common, but it is considered one of the deadliest cancers. According to the latest estimates of the American Cancer Society, 16,470 people in the United States were diagnosed with esophageal cancer and 14,530 died of the disease in 2009. The 5-year overall survival rate is only 18%, according to the Surveillance, Epidemiology, and End Results Program of the U.S. National Cancer Institute.

One of the reasons for the low survival rate of patients with this cancer is that it is often advanced before it is found. Two factors contribute to the likelihood of late detection: First, esophageal cancer does not cause alarming early symptoms; the most common presenting symptom is dysphagia. Typically, the dysphagia is progressive and easily ignored, and consultation is not sought until the patient has difficulty swallowing soft foods or even liquids, by which time the lumen of the esophagus is often substantially obstructed by the tumor.

The second factor is the anatomy of the esophagus itself. Unlike the rest of the gastrointestinal tract, the esophagus lacks a serosal layer of tissue, making it more vulnerable to local invasion by cancer cells. The esophagus is also richly supplied by adjacent lymphatics, which provide a conduit for rapid spread of cancer cells to regional cervical, mediastinal, paraesophageal, gastric, and celiac lymph nodes. As a result,

esophageal cancer is associated with early invasion of adjacent structures—including the pericardium, heart, trachea, vertebral body, and lung—and early metastasis, most commonly to the lung, liver, and bone. In fact, regional lymph node involvement is found in more than 75% of esophageal cancer patients at presentation, according to Steven Hsesheng Lin, M.D., Ph.D., an assistant professor in the Department of Radiation Oncology at The University of Texas MD Anderson Cancer Center.

Over the past 2 decades, there has been a dramatic shift in incidence of histologic type and tumor location for esophageal cancers in the United States. Prior to the 1990s, squamous cell carcinoma was the predominant histology, and it is still the most common worldwide. But in the United States, adenocarcinomas have become the most common, and in fact, adenocarcinoma of the esophagus has the fastest growing incidence rate of all cancers.

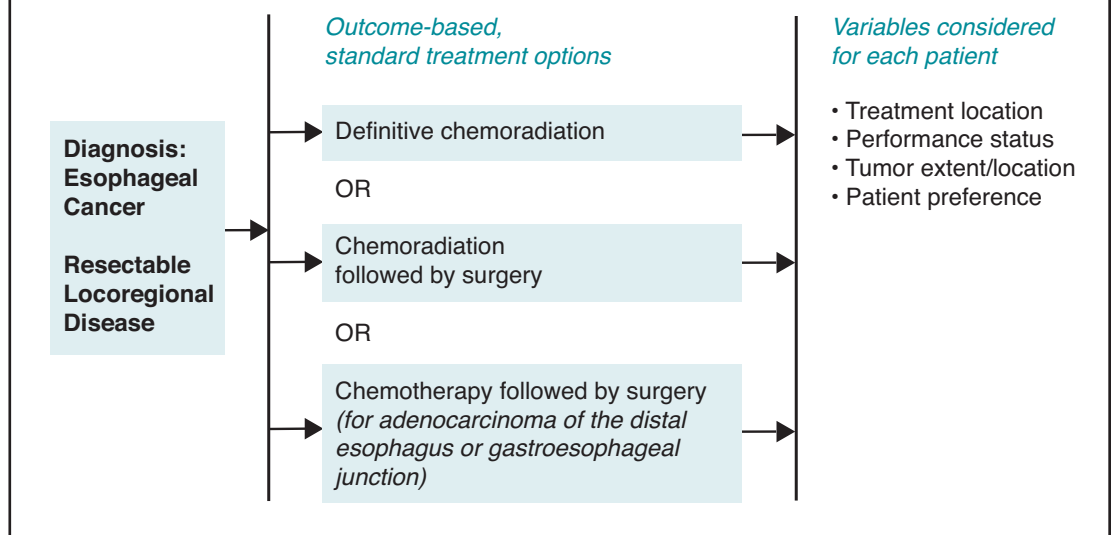
The primary risk factors for squamous cell cancers of the esophagus are tobacco and alcohol use. These cancers are also associated with achalasia, lye strictures, and therapeutic radiation as well as Plummer-Vinson syndrome (a condition characterized by dysphagia and esophageal webs) and tylosis (a hereditary cutaneous disorder). Squamous cell carcinomas can occur in any location within the esophagus. Adenocarcinomas, on the other hand, tend to occur in the distal esophagus and at the gastroesophageal junction and are strongly associated with chronic gastrointestinal reflux and obesity. Barrett esophagus is also considered a strong risk factor for adenocarcinoma of the esophagus.

### Treatment Overview

The cornerstone of curative treatment for esophageal cancer has traditionally been surgery (esophagectomy). Thus, a primary objective of the initial patient evaluation is to determine whether the disease is resectable. According to Stephen Swisher, M.D., a professor in and chairman of the Department of Thoracic and Cardiovascular Surgery, the major technical barrier to resectability in the thorax is tumor involvement of the aorta or tracheobronchial airways. Even if the tumor is resectable, circumferential margins are often very close owing to the proximity of critical surrounding structures. Because of this, preoperative chemoradiation has been used in conjunction with surgery to help achieve complete resections with uninvolved proximal, distal, and circumferential margins.

Esophagectomy is a major and complex operation in which

## Primary Treatment Options for Resectable Locoregional Cancer of the Esophagus



the tumor-bearing esophagus is removed and the alimentary tract is reconstructed using the stomach or, in some cases, the intestine. One potentially serious complication is an anastomotic leak, which has led to the high morbidity and mortality rates historically associated with this surgery. Morbidity and mortality have been reduced in recent years by high-volume centers specialized in esophageal resection. Referral of esophageal cancer patients to a high-volume center is therefore recommended.

Surgery alone, however, has proven curative in only 20% of patients with locoregional esophageal cancers, suggesting that microlymphatic disease is probably present in most cases and that additional therapy is needed to achieve both regional and distant disease control. Radiation therapy and chemotherapy have been studied alone and as single adjuncts to surgery, given either preoperatively (neoadjuvantly) or postoperatively, but the most significant improvements in survival have been seen using both.

Although large trials to date have not proven chemotherapy plus radiation therapy given preoperatively to be superior to that given postoperatively, there is a strong rationale for preoperative use. “The whole idea behind adjuvant therapy is to manage occult distant disease,” said Linus Ho, M.D., Ph.D., an associate professor in the Department of Gastrointestinal Medical Oncology. “But valuable time passes if we wait until after surgery and surgical recovery, so we prefer neoadjuvant therapy because it addresses occult disease earlier.” Dr. Ho also noted that the adjuvant treatment is better tolerated before surgery. “In fact, among patients who have surgery first, 30%–50% will never receive postoperative therapy because it is more difficult to tolerate after surgery,” he said. “And that represents a lost opportunity.” According to Dr. Ho, there is an additional benefit to neoadjuvant therapy: improvement of symptoms. Many patients present with substantial esophageal obstruction as well as weight loss and nutritional deficits. Some require temporary gastrostomy or jejunostomy tubes to provide nutritional support via enteral feedings, but by the end of chemoradiation treatments, many such patients are able to eat normally.

Given the advantages of neoadjuvant therapy, the current standard recommendations for patients with locoregional disease include chemoradiation alone or chemoradiation followed by surgery. Chemotherapy followed by surgery is also consid-

ered a standard for adenocarcinomas in the distal esophagus or gastroesophageal junction, but at MD Anderson, combined-modality neoadjuvant treatment is favored over neoadjuvant chemotherapy for these patients, too. “Based on large studies and our own experience, neoadjuvant chemoradiation is our preferred approach,” Dr. Lin explained. He pointed out that some of the large European trials showing significant results with neoadjuvant or perioperative chemotherapy (without radiation) included gastric cancers in the study population, which may account for the difference in results from other studies and the experience at MD Anderson.

### Treatment Decisions

The primary treatment decision for patients presenting with locoregional esophageal cancer is whether to employ chemoradiation alone or to follow it with surgery. Overall, survival rates are superior when surgery is included. However, because esophagectomy is a major and complex surgery, the decision for individual patients can vary. In addition, chemoradiation alone is curative in 25% of patients—this was demonstrated in a large trial (Radiation Therapy Oncology Group [RTOG]-8501) that compared chemoradiation alone to radiation alone in patients with unresectable esophageal cancer and further corroborated by the observation of complete pathologic responses in 25% of patients after chemoradiation therapy. Clearly, there are some patients who do not require surgery. “The problem is that we don’t know ahead of time which patients those are,” said Dr. Lin, pointing out that the remaining 75% of patients who receive chemoradiation alone have varying degrees of residual disease (from 1%–80%). When there is a complete response to therapy, long-term overall survival is greater than 60%.

In general, one of the primary considerations in the esophagectomy decision is where the surgery will occur—specifically, whether the patient will be treated at a center that performs a

(Continued on page 6)

high volume of esophagectomies. Numerous studies have confirmed that mortality rates from various surgeries are related to the volumes of those surgeries performed at an institution. Esophagectomy is a surgery for which the difference in mortality rates between high- and low-volume centers is marked, with high mortality rates in centers where few procedures are performed. Surgeon experience and the availability of supportive perioperative care, including specialty services to detect and manage leaks should they occur, are critical factors. Access to a high-volume center is therefore an important risk consideration.

At MD Anderson, the medical decision between trimodality therapy or chemoradiation alone hinges primarily on the patient's performance status—which indicates how well surgery will be tolerated—and on the relative risk of recurrence. Patients who are otherwise in poor health or who have comorbidities that would compromise recovery are often better suited to receive chemoradiation alone. But for patients who are healthy and good surgical candidates, the question of whether to have surgery is a personal one that requires substantial discussion between physician and patient.

Should a locoregional recurrence occur later, it may be more difficult to resect completely. "For some patients, this might mean that we missed an opportunity for a cure while disease was at an earlier stage," said Dr. Swisher. On the other hand, the surgery requires a substantial recovery period and lifestyle changes—for example, eating smaller, more frequent meals—that may factor into the decision. "Patients usually make these adjustments and over time don't find them to be major problems," Dr. Swisher said, "but these lifestyle changes are something that we discuss."

Dr. Swisher spends a considerable amount of time ensuring that patients are fully informed and comfortable with their decision. "Some patients don't want to take any chances—they want to do everything possible up front to get rid of their cancer and minimize the possibility of the cancer returning," he said. "Others would like to avoid the surgery if they possibly can, and we assure them that this approach is also reasonable." The size and extent of tumor may also play a role in the decision if they influence the complexity and risk of the surgery.

A large clinical trial (RTOG-0246) recently completed sheds some additional light on the appropriateness of "selective surgery." In this trial, patients received induction chemotherapy followed by definitive chemoradiation and were monitored thereafter at 3-month intervals with computed tomography and positron emission tomography if no disease was detected after chemoradiation. Surgery was done only if residual or recurrent disease was detected. In the study, about 40% of patients were found to have residual disease following chemoradiation. Of the remaining 60%, about 10%–20% had a recurrence requiring surgery and another 20% had dis-

tant recurrence and therefore may not have benefitted from esophagectomy anyway. "For those patients who ultimately need delayed surgery, the risks may go up because of the delay, particularly for complications such as anastomotic leaks. Because of this and the high risk of residual disease, we still recommend planned surgery for patients who are physically fit, although selective surgery is always offered as an option," Dr. Swisher said.

Another initiative that holds promise for making the treatment decision easier is aimed at identifying the 25% of patients in whom chemoradiation will result in a cure. According to Dr. Lin, post-treatment biopsies are not reliable predictors of pathologic response, and although better outcomes are seen in patients who have a complete response to chemoradiation as gauged by imaging, the possibility of residual disease cannot be ruled out by imaging. Dr. Lin believes that the key to identifying patients who can be cured by chemoradiation lies in understanding the molecular biology of tumor subtypes and identifying the phenotypic signature of those tumors likely to have a complete response to chemoradiation. Current studies are using genetic profiling techniques to analyze tissues from pretreatment endoscopic biopsy specimens, and molecular subtypes of esophageal cancer have been identified.

"We hope this leads to the identification of biomarkers that will enable us to predict those patients who will have complete responses to neoadjuvant therapy and can thus safely forego surgery," Dr. Lin said. ●

## References

National Comprehensive Cancer Network: Clinical Practice Guidelines in Oncology, Esophageal Cancer V1.2010; [http://www.nccn.org/professionals/physician\\_gls/PDF/esophageal.pdf](http://www.nccn.org/professionals/physician_gls/PDF/esophageal.pdf)

### Contributing Faculty The University of Texas MD Anderson Cancer Center



**Linus Ho, M.D., Ph.D.**  
Associate Professor, Gastrointestinal Medical Oncology



**Steven Hsheng Lin, M.D., Ph.D.**  
Assistant Professor, Radiation Oncology



**Stephen G. Swisher, M.D.**  
Professor and Chair, Thoracic and Cardiovascular Surgery



# Understanding Clinical Trials

**N**ew cancer treatments typically undergo years of testing before they are approved for standard use in people. One of the last steps in this testing process is the clinical trial, a controlled study of how a new treatment works in patients.

Cancer clinical trials take place in four phases. Each phase asks different questions and gathers data to support further research. The phase indicates how much research has been done and approximately how many people have participated in the study.

## Phase I trials

Phase I trials usually test a new treatment in humans for the first time, after the treatment has been shown to be safe and effective in laboratory and animal studies. A phase I trial can also be used to evaluate an approved drug at higher doses or in a different disease. Fifteen to 20 people usually participate, and patients with different types of cancer might be allowed to enter the trial. These patients have usually tried other treatments without success.

In phase I trials, researchers focus on the safety of the treatment, studying the best way to administer the new treatment, the maximum safe dose, and how often the treatment should be given. One of the benefits of participating in a phase I trial is being among the first to receive a new treatment that might prove effective against cancer. However, phase I trials also carry risks, since the effectiveness of the treatment in people has not been demonstrated and no one yet knows what side effects might occur.

## Phase II trials

If the new treatment is shown to be safe in a phase I trial, the study progresses to phase II. In phase II trials, researchers continue to test the safety of



**Clinical trials are controlled studies of how new treatments work in patients.**

a new treatment and begin to evaluate how well it works at different doses. These trials enroll fewer than 100 participants, and eligibility is usually based on prior treatment. Recruiting enough participants for a phase II trial may take up to 2 years.

## Phase III trials

Treatments that are shown to be effective in phase II trials are further refined and studied in phase III trials. Phase III trials, which compare a new treatment with the standard treatment for a particular disease, typically enroll between 100 and several thousand people. Participants are divided into two or more study groups, depending on the research questions being asked. Despite a popular misconception, placebos are rarely used in cancer treatment trials. Researchers instead try to find out whether the new treatment works better than, the same as, or worse than the

standard treatment in participants ranging from newly diagnosed patients to people with advanced disease.

Even though about half the patients in a phase III trial will not get the new treatment, those who don't will receive the standard treatment, which has so far been proven to be the best available. Risks can include adverse effects that were not noted in prior studies or are worse than those found in standard treatment. It is also possible that the new agent will be less effective than the standard treatment. Recruitment for phase III trials can take 3 to 4 years.

## Phase IV trials

Phase IV trials are rare. They are conducted after a new treatment has been approved for standard use and are used to measure the long-term safety and effectiveness of the treatment.

## Patient participation

After receiving a thorough explanation of the possible risks and benefits of the treatment being studied, the patient should always be the one to decide whether to participate in a clinical trial. It is the responsibility of each research center's institutional review board to ensure that all clinical trials include treatments that are at least as good as standard care. Patients who choose to take part in clinical trials may or may not receive a benefit beyond what they would have received with standard care, but their participation will add to what is known about their disease and perhaps lead to a cure. ●

*For more information, talk to your physician, or:*

- visit [www.mdanderson.org](http://www.mdanderson.org)
- call askMDAnderson at 1-877-632-6789

**OncoLog, July 2010**

©2010 The University of Texas  
MD Anderson Cancer Center

**Address Service Requested**

## Refining Approaches to Thyroid Cancer

(Continued from page 3)

for 3 or 4 years now, maintaining stable disease.” However, Dr. Sherman said, “It is important to recognize that we have not seen complete remissions, and we don’t have any data yet that say patients live longer. So these drugs and their clinical trials are still focused on patients with significantly progressing disease and are not appropriate for typical patients with metastatic thyroid cancer that’s indolent or asymptomatic.”

Other drugs that have already been approved for other cancers, including sorafenib and sunitinib, are being offered off-label to selected patients with progressive disease who need further therapy but are ineligible for or unwilling to participate in clinical trials.

Dr. Sherman said that identifying combinations of targeted therapies or combinations of targeted therapy and traditional cytotoxic therapy may not just control disease but eliminate it.

“The challenge will be identifying treatments that are safe enough and effective enough that we can move the starting point for therapy with targeted agents up earlier in the course of people’s disease,” Dr. Sherman said. “Seven years ago, we couldn’t convince anybody to support a thyroid cancer trial. Now, we have the luxury to prioritize what we do, and we have a range of phase I through phase III studies to cover a broad array of patients.”

### Multidisciplinary approach

In treating thyroid cancer patients, Dr. Clayman and Dr. Sherman agree that a multidisciplinary approach is ideal, not just for the initial treatment, but also for patients’ long-term care.

“Our greatest strength at MD Anderson is an amalgamated team of cytologists, ultrasonographers, cross-sectional imaging technologists, surgeons, endocrinologists, radiation therapists, and oncologists who specialize in thyroid cancer management,” Dr. Clayman said. “Patients who may benefit from such a programmatic evaluation are best referred early on.”

Dr. Sherman said, “We obviously strongly believe in the value of a multidisciplinary approach and having patient care not just delivered by but also discussed collectively among endocrinologists, surgeons, oncologists—the full range of specialists. One can argue that for many patients with low-risk thyroid cancer the kind of multidisciplinary approach that we take is not essential. But for the sort of patients we increasingly see here—with locally invasive and metastatic disease—it’s absolutely essential that they be treated in a multidisciplinary environment.” ●

*For more information, contact Dr. Sherman at 713-792-2841 or Dr. Clayman at 713-792-8837. For information about clinical and laboratory studies in thyroid cancer, visit [www.mdanderson.org/oncolog](http://www.mdanderson.org/oncolog).*

# OncoLog

The University of Texas  
MD Anderson Cancer Center

#### President

John Mendelsohn, M.D.

#### Provost and Executive Vice President

Raymond DuBois, M.D., Ph.D.

#### Senior Vice President for Academic Affairs

Stephen P. Tomasovic, Ph.D.

#### Director, Department of Scientific Publications

Walter J. Pagel

#### Managing Editor

John LeBas

#### Assistant Managing Editors

Joe Munch

Bryan Tutt

#### Contributing Editors

Melissa G. Burkett

Lionel Santibañez

Sunni Hosemann

Ann M. Sutton

#### Design

Janice Campbell, The Very Idea®

#### Editorial Board

Michael Fisch, M.D., Chair

Lyle Green, Vice Chair

Therese Bevers, M.D.

Robert Gagel, M.D.

Beverly Handy, M.D.

Patrick Hwu, M.D.

Charles Koller, M.D.

Maurie Markman, M.D.

Shreyaskumar Patel, M.D.

David Schwartz, M.D.

Rena Sellin, M.D.

Randal Weber, M.D.

Christopher Wood, M.D.

**Physicians:** To refer a patient or learn more about MD Anderson, please contact the Office of Physician Relations at 713-792-2202, 1-800-252-0502, or [www.physicianrelations.org](http://www.physicianrelations.org).

**Patients:** To refer yourself to MD Anderson or learn more about our services, please call 1-877-632-6789 or visit [www.mdanderson.org](http://www.mdanderson.org).

For questions or comments about *OncoLog*, please e-mail [scientificpublications@mdanderson.org](mailto:scientificpublications@mdanderson.org) or call 713-792-3305. Current and previous issues are available online in English and Spanish at [www.mdanderson.org/oncolog](http://www.mdanderson.org/oncolog).

Made possible in part by a gift from the late Mrs. Harry C. Wiess.

**NCI**® A Comprehensive Cancer  
**CCC** Center Designated by the  
National Cancer Institute