

Treating Cancer in Pregnant Patients

By Bryan Tutt

Pregnancy is usually a joyous, hopeful time; a cancer diagnosis can be devastating. When pregnancy and cancer occur together, they present special challenges for patients and physicians. Fortunately, these challenges often can be overcome by a multidisciplinary approach to treatment.

"Cancer treatment is not incompatible with pregnancy," said Andrea Milbourne, M.D., head of the Section of General Gynecology and an associate professor in the Department of Gynecologic Oncology and Reproductive Medicine at The University of Texas MD Anderson Cancer Center. "The old idea that a pregnant patient has to choose between terminating the pregnancy and going without treatment isn't true in most cases."

According to Dr. Milbourne, cancer affects about 1 in 1,000 pregnant women. Breast cancer, leukemia, lymphoma, and malignant melanoma are the cancers that occur most often in pregnant women.

Breast cancer

"The speculation is that breast cancer occurs more frequently during pregnancy than other cancers because many women are delaying childbearing until their 30s, when breast cancer incidence goes up," said Richard L. Theriault, D.O., a professor in the Department of Breast Medical Oncology.

About 1 in 3,000 pregnant women are believed to have concurrent breast cancer.

Diagnosis and workup

Dr. Theriault said that most patients with concurrent pregnancy and breast cancer learn they are pregnant before they are diagnosed with cancer. Although women are sensitive to changes in their breasts during pregnancy and likely to notice any new lumps, these lumps are sometimes mistaken for blocked milk ducts or inflammation, which could delay correct diagnosis.

"The standard of care is the same for pregnant

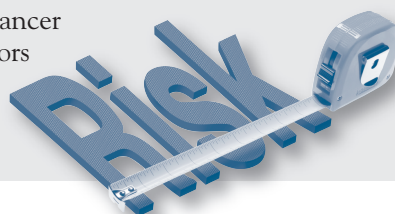
██████████ was diagnosed with breast cancer and began chemotherapy while pregnant.

**Compass: Stage IIIA
Non-Small Cell Lung Cancer**
Many factors affect treatment decisions

4

House Call
Understanding cancer risk and risk factors

7



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Treating Cancer in Pregnant Patients

[Continued from page 1]

women as for nonpregnant women,” Dr. Theriault said. “Any time there is an abnormality in the breast that’s been there more than 2 weeks, it needs to be subjected to imaging of some type.” He said this usually includes diagnostic mammography and ultrasonography of the breast. Although the radiation dose from mammography is negligible, shielding is typically provided to protect the fetus.

If imaging suggests a mass may be cancer, a core needle biopsy is performed. If the initial ultrasound examination indicates lymph node involvement, a fine needle aspiration biopsy of the lymph nodes is done as well. Both these procedures can be done safely in pregnant women.

“In our population of pregnant women, 65%–70% have lymph node involvement at the time of diagnosis,” Dr. Theriault said. “If the lymph nodes are involved or if there is reason to suspect metastasis, we look for other organ systems that might also be involved—especially in women with symptoms like back pain or belly pain.”

Breast cancer is often found at later stages in pregnant women than it is typically found in nonpregnant women. “This may be due to younger age of the pregnant patient population and to changes in the breast occurring during pregnancy,” said Jennifer K. Litton, M.D., an assistant professor in the Department of Breast Medical Oncology. “We follow guidelines for evaluation of distant disease similarly in pregnant and nonpregnant women, but we modify the imaging due to the pregnancy.”

The common sites of breast cancer metastases are the same in pregnant women and nonpregnant women: lungs, liver, and bones. Chest radiography is used to screen for breast cancer metastases in the lungs; as with mammography, this procedure does not expose the fetus to dangerous levels of radiation, and shielding can be provided. Ultrasonography is used to check for liver metastases. Non-contrast-enhanced magnetic resonance imaging of the thoracic and lumbar spine is used to assess for bone metastases. Dr. Theriault said the accuracy of this imaging modality

has been shown to be the equivalent of bone scintigraphy, which is avoided in pregnant women because it irradiates the fetus.

“We see the patient and stage the cancer, and then we determine the best treatment for the patient’s cancer while monitoring the fetus closely as well,” Dr. Litton said.

Treatment

The most important concern about treating pregnant cancer patients is avoiding chemotherapy during the first trimester, when the risk of organ malformation in the fetus is greatest.

After the first trimester, pregnant women receive a standard chemotherapy regimen—5-fluorouracil, doxorubicin, and cyclophosphamide—similar to that given to nonpregnant women with breast cancer.

The use of taxanes typically is delayed until after the baby is delivered because of concerns that the high levels of cytochrome P-450 in pregnant women might increase the metabolism of these drugs, potentially limiting their effectiveness.

Likewise, trastuzumab, which is used to treat HER2-positive breast cancer, is given only after delivery. “We don’t want to give chimeric antibodies during pregnancy because there is concern that they could cross the placenta and cause fetal abnormalities or abnormal fetal development,” Dr. Milbourne said. Endocrine therapy with tamoxifen also is not given during pregnancy because it has been associated with birth defects.

Surgery can be done safely during pregnancy. As in nonpregnant patients, pregnant patients typically undergo mastectomy, partial mastectomy, or lumpectomy before or after chemotherapy.

“We prefer to use a team approach to treatment,” Dr. Theriault said. “We work with the Department of Clinical Cancer Genetics because most of these patients are in their 30s, so we want to look at their *BRCA1* and *BRCA2* risks. We communicate with our patients’ obstetricians and with the fetal medicine specialists at the Department of Maternal-Fetal Medicine at The University of Texas Health Science Center

at Houston. Surgical oncologists see these patients early, and if we think radiation therapy will be needed after delivery, patients see a radiation oncologist early as well.”

Doctors prefer not to administer radiation therapy during pregnancy because of the proximity of the breast to the fetus. However, Dr. Litton said, “Radiation therapy for breast cancer is typically given after chemotherapy and surgery, and by that time, the baby has been delivered.”

The child’s health

“Our primary focus is treating the patient and her cancer, but we want a healthy baby as well,” Dr. Theriault said. “We always require an evaluation of the mother and the fetus by a maternal-fetal medicine specialist. Generally speaking, we want to have that done before every cycle of chemotherapy. That way, we can monitor the growth and development of the baby and we can plan for when delivery might occur.”

Dr. Milbourne said, “Depending on how long chemotherapy is given, delivery may need to be carefully scheduled, so communication between the treating obstetrician and the treating oncologist is very, very important. Many chemotherapeutic agents lower patients’ white blood cell and platelet counts, and this can be dangerous to the mother and the baby during delivery.”

Dr. Theriault was the principal investigator for a clinical trial in which pregnant women are treated for breast cancer and monitored to determine their long-term outcomes and the health of their children; Dr. Litton has since assumed the role of principal investigator. About 80 women have been treated since the trial began enrolling patients in 1989. “Our data show that pregnant patients do as well as nonpregnant patients and that the children’s health seems to be right on par with that of the general population,” said Dr. Litton. “We’ve had three children out of those 80 with congenital malformations, and in the general population the risk is 3%–4%.” In fol-

A Success Story

██████████ was 5 months' pregnant when she noticed soreness in her left breast. This was her third pregnancy, and the soreness was different and more severe than in her previous pregnancies.

██████████ obstetrician first suspected mastitis and prescribed antibiotics. When these had no effect, the obstetrician ordered an ultrasound study, which detected a mass in the breast that biopsy confirmed as cancer. ██████████ traveled to Houston and was treated by Dr. Jennifer Litton at MD Anderson.

"Treatment wasn't that bad," ██████████ said. "My mom and my sister-in-law both went through breast cancer treatment, and my protocol was the same as theirs. The side effects weren't any more severe than what they described." ██████████ pregnancy was monitored by a maternal-fetal medicine specialist from The University of Texas Health Science Center at Houston. Before every chemotherapy session, ██████████ would undergo ultrasonography to assess fetal fluids and growth.

██████████ gave birth to a healthy baby girl and afterward continued chemotherapy. At the time this article was printed, her treatment was going well, and she was scheduled to return to MD Anderson for surgery and radiation therapy. ■

low-up surveys, only allergies and eczema were more prevalent in the children of mothers treated in the trial than in the general population. And these differences could be the result of reporting bias.

Other cancers in pregnant patients

In addition to those with breast cancer, Dr. Milbourne sees pregnant patients with various other cancers. "Some of these cancers are found during pregnancy because pregnant women are under more intense scrutiny by physicians during pregnancy," she said. "We've had patients whose leukemia was detected by blood work done during pregnancy."

Dr. Milbourne said that the unique aspects of each patient's pregnancy and cancer must be considered. For example, she said that women diagnosed with leukemia during the early trimesters of pregnancy usually do poorly because the low white blood cell and platelet levels associated with treatment can lead to infections or because high white blood cell levels in untreated patients pose a potential threat to the fetus. However, she added, "We've had a few who were treated successfully. We had one woman with chronic myelogenous leukemia who was treated with leukapheresis during pregnancy, and once the baby was delivered she was able to proceed with her definitive treatment."

Cervical cancer is relatively rare in pregnancy; however, cervical dysplasia (precancerous changes in the epithelial cells of the cervix) is sometimes detected in pregnant women. "If a woman has an abnormal Papanicolaou test during pregnancy, we order a colposcopy, but if it doesn't look like cancer, no biopsy is done until after the baby is delivered," Dr. Milbourne said. If the cancer is in an early stage, it can be treated by surgery—a trachelectomy—without harm to the fetus. If the cancer is further along, radiation therapy and chemotherapy are the standard treatment. Because radiation therapy to the cervix would be lethal to the fetus, the pregnancy would need to be terminated before the treatment began.

In fact, radiation therapy for any type of cancer usually is avoided during pregnancy. "We have some patients who have had radiation therapy for head and neck cancers while pregnant with good results. But despite shielding to protect the fetus and despite the precision of these treatments, there is a certain amount of radiation scatter that could pose a risk," Dr. Milbourne said.

Likewise, some pregnant patients with lymphoma have been successfully treated with radiation, but when possible radiation therapy for lymphoma is postponed until after delivery. In lymphoma and myeloma patients, many of the standard chemotherapeutic drugs can be given during the second and third trimesters of pregnancy. As in

patients with breast cancer, treatment with monoclonal antibodies during pregnancy typically is avoided in these patients.

Cutaneous melanoma can be safely removed during pregnancy. Although surgery that does not involve the abdomen can be done safely in any trimester of a patient's pregnancy, many doctors prefer to postpone surgical procedures until after the first trimester if possible because the risk of miscarriage is highest during the first trimester.

Treatment decisions

Ultimately, the decisions about cancer treatment during pregnancy rest with the patient. Her physicians need to discuss with her in detail the risks and benefits of all her cancer treatment options. "Some women will choose to terminate the pregnancy and focus on fighting their cancer; others will refuse any treatment until after the baby is born. We respect the patient's decision," Dr. Milbourne said. She added that treatment recommendations should include input from specialists involved in all aspects of the patient's care. "Every patient needs to be looked at on an individual basis. If in doubt, get a second opinion; get a third opinion." ■

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Compass

Quarterly discussion of cancer types for which there is no standard treatment or more than one standard treatment

Non–Small Cell Lung Cancer: Stage IIIA

Many factors affect treatment sequence

By **Sunni Hosemann**

Introduction

The two major categories of lung cancer defined by the World Health Organization—small cell lung cancer and non–small cell lung cancer (NSCLC)—have different biological behaviors and are staged and treated differently. NSCLC is by far the more prevalent of the two, accounting for 85%–90% of diagnosed lung cancers.

This discussion is limited to NSCLC and will focus on stage IIIA as its treatment is the most controversial among lung cancers. Stage IIIA NSCLC is by no means homogeneous; within this stage, there is a wide range of primary tumor sizes and distribution, disease spread into the mediastinum may be absent or pronounced, and there may be variable involvement of the lung and/or surrounding structures. These factors have significant implications for treatment choices.

According to Anne Tsao, M.D., an associate professor in the Department of Thoracic/Head and Neck Medical Oncology at The University of Texas MD Anderson Cancer Center, most patients with stage IIIA NSCLC require all three major cancer treatment modalities—surgery, radiation therapy, and chemotherapy. “Determining the order in which these should be given is the challenge,” she said.

The roles and timing of chemotherapy and radiation therapy—whether they will be given concurrently or sequentially and whether they will be given as definitive treatment or adjuvant treatment before or after surgery—are best determined before any treatment begins. According to Melenda Jeter, M.D., an associate professor in the Department of Radiation Oncology, these are important considerations because different doses and regimens are used for each scenario. For example, if chemoradiation is given as preoperative treatment, lower doses of radiation are necessary than would be used if chemoradiation is given as the definitive treatment. Similarly, if chemotherapy and radiation therapy are administered concurrently, the toxicity of the treatments may necessitate giving lower doses of each than if they were given sequentially.

When a patient’s disease is classified as stage IIIA before any treatment begins, surgery is rarely the preferred initial treatment, even if the disease is deemed operable. According to the National Comprehensive Cancer Network, approximately half of its member institutions favor chemoradiation as the first treatment, and the other half prefer chemotherapy first. At MD Anderson, chemotherapy is preferred as the initial treatment. The rationale for this is discussed below.

Treatment decisions

The keys to the optimal treatment sequence for any patient with NSCLC are a very thorough pretreatment staging evaluation and a multidisciplinary consultation that includes medical, radiation, and surgical oncologists. The treatment decisions for a given patient with stage IIIA NSCLC are whether surgery will be part of the treatment plan, whether chemotherapy and radiation therapy will be definitive or adjuvant treatments, whether chemotherapy and radiation therapy will be given concurrently or sequentially, and whether chemotherapy and radiation therapy will be given neoadjuvantly or adjuvantly if surgery is done.

Neoadjuvant therapy

When a patient’s disease is deemed resectable or potentially resectable, neoadjuvant therapy is the next consideration. Although neoadjuvant chemotherapy and chemoradiation are generally considered equivalent, at MD Anderson, chemotherapy is preferred over chemoradiation as a preoperative treatment for the following reasons:

- A higher chemotherapy dose can be used if chemotherapy is given alone than if combined with radiation therapy. The higher dose is more likely to control micrometastases, which if present could ultimately override any benefit of radiation and surgery, which are local therapies.
- Chemoradiation prior to surgery requires that a smaller dose of radiation be used than would be used as a definitive treatment. If further radiation therapy is to be given after surgery, a break in therapy is required for an undetermined time period. This limits the ability to give a definitive dose and should be avoided if possible, according to Dr. Jeter. “Instead, we prefer to give treatment without breaks and either give definitive radiation therapy or reserve it for use postoperatively where needed,” she said.



Wayne L. Hofstetter, M.D.
Associate Professor, Thoracic
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Medical Oncology

- Chemotherapy as an induction therapy allows for reassessment of mediastinal disease and perhaps reconsideration of a surgical option in patients who have a response. A patient whose disease does not respond appropriately or progresses during induction chemotherapy would not have benefited from surgery. "Induction chemotherapy doesn't burn any bridges," said Wayne Hofstetter, M.D., an associate professor in the Department of Thoracic and Cardiovascular Surgery. "It doesn't preclude any other treatment as a potential next step for an individual patient."

Is surgery feasible?

The role of surgery in stage IIIA NSCLC is one of the most controversial issues in cancer treatment. "Surgery is not appropriate for all patients," Dr. Hofstetter said. "Stage IIIA NSCLC is diagnosed in a very heterogeneous group of patients—the presentation varies by tumor size and location and by the amount and distribution of disease, in lymph nodes for example. These factors influence whether surgery will be helpful."

A thoracic surgical oncologist must therefore determine whether the patient is medically able to tolerate the required surgery and whether the disease can be removed with acceptable margins and with sufficient functional lung for adequate pulmonary reserve remaining postoperatively.

Today's imaging technologies make more accurate pretreatment staging possible than was available in the past and enable better treatment sequences to be planned for individual patients—maximizing the potential efficacy of each modality while avoiding treatments that will not help. At MD Anderson, positron emission tomography (PET) and PET/computed tomography imaging and endobronchial ultrasonography with fine-needle aspiration biopsy are used for the pretreatment workup. Mediastinoscopy is added if needed to verify whether there is disease in the mediastinal lymph nodes. "It is very important to have a proven diagnosis before we treat," Dr. Hofstetter said. Noting that chronic inflammation or histoplasmosis (more common in the southern United States) can cause false-positive lymph nodes on PET scans, he recommends that histological confirmation of NSCLC be obtained before a patient undergoes any treatment. "We also want to rule out IIIB disease—contralateral lymph node involvement—for which surgery is not helpful."

Dr. Hofstetter believes that surgery is most helpful where

STAGE IIIA NON-SMALL CELL LUNG CANCER: Standard Options

Diagnosis:
**Non-Small Cell
Lung Cancer**

Stage IIIA
T1–4, N0–2, M0

Variables Considered for Each Patient

- Tumor resectability
- Performance status
- Tumor size
- Tumor location
- Tumor histology
- Lymph node status

Outcome-Based, Standard Initial Treatment Options

Definitive
chemoradiation

OR

Induction
chemoradiation followed
by surgery

OR

Induction chemotherapy
followed by surgery
and/or radiation therapy

mediastinal disease is absent or there is nonbulky mediastinal disease with few lymph node stations affected. For multistation or bulky mediastinal disease, surgery is less effective and, if considered, would be preceded by chemotherapy and/or radiation therapy. Further, he noted that when pneumonectomy would be necessary for complete resection in a patient with stage IIIA N2 disease, definitive nonsurgical treatments should be considered instead, citing unacceptable surgical mortality rates associated with pneumonectomy—particularly when performed after chemoradiation.

Dr. Hofstetter further noted that if surgery is done, it must include appropriate lymph node dissection of all reachable mediastinal stations. "It is never appropriate to forego a thorough evaluation of lymph node stations," he said.

Definitive chemoradiation

Patients who are not surgical candidates should receive definitive chemoradiation. Whether chemotherapy and radiation therapy are given concurrently or sequentially must be determined for each patient. According to Dr. Jeter, as a definitive treatment, concurrent chemoradiation is more effective than chemotherapy followed by radiation therapy but is also more toxic and is associated with higher rates of grade 3 or 4 esophagitis than sequential therapy, so patient tolerance becomes a consideration. She noted that many patients who are unable to tolerate concurrent therapy are also unable to tolerate sequential therapy, so radiation therapy alone or combined with targeted therapies might be considered for them.

According to Dr. Jeter, radiation for lung cancers is prefer-

ably given with intensity-modulated radiation therapy (IMRT) or, more recently, proton therapy, as lung tissue is very sensitive and surrounded by critical structures (the heart, esophagus, and spinal cord). “This is particularly true where there is bulky or central disease, the patient has cardiac disease, or the patient had previous radiation to the area—for breast cancer, for example—and we want to avoid re-irradiating tissues,” she said. A trial to compare proton therapy with IMRT is currently accruing patients with unresectable stage II or III NSCLC, or stage IV NSCLC with treated solitary brain metastasis; the study is being done at MD Anderson and Massachusetts General Hospital.

Chemotherapy

“In the adjuvant therapy trials where systemic chemotherapy is given, there is an increase of about 5% in 5-year overall survival rates,” Dr. Tsao said.

Chemotherapy—whether given neoadjuvantly alone or with radiation or given postoperatively—is tailored to tumor histology. Chemotherapy regimens administered with curative intent usually include a platinum-based drug paired with another agent, but future regimens may ultimately incorporate targeted therapies. “We know that certain chemotherapies and targeted agents work only with certain

[Continued on page 8]

Lung Cancer Staging

The American Joint Committee on Cancer staging system differentiates cancer stages by tumor size (**T**), lymph node involvement (**N**), and presence of distant metastasis (**M**), to classify disease into groups with prognostic significance and treatment implications. For non-small cell lung cancer (NSCLC), the TNM classifications are defined as follows:

T classification includes not just tumor size but also the location and the extent of spread to specific nearby structures. For NSCLC, these classifications include:

- T1, the tumor is 3 cm or less in diameter, has not reached the visceral pleura, and does not affect the main branches of the bronchi;
- T2, the tumor is 3–7 cm in diameter, or it involves a main bronchus but is not closer than 2 cm to the carina, or it has grown into the visceral pleura, or it obstructs the airways but has not caused the entire lung to collapse or develop pneumonia;
- T3, the tumor is larger than 7 cm in diameter; or it has grown into the chest wall, diaphragm, mediastinal pleura, or parietal pericardium; or it invades a main bronchus and is closer than 2 cm to the carina but does not involve the carina itself; or it obstructs the airways enough to cause an entire lung to collapse or develop pneumonia; or two or more tumor nodules are present in the same lobe of a lung;
- T4, the tumor has grown into the mediastinum, heart, large blood vessels near the heart, trachea, esophagus, spine, or carina; or two or more separate tumor nodules are present in different lobes of the same lung.

N classification describes not just the number of involved lymph nodes but also their location. For NSCLC, the N classifications are:

- N1, lymph nodes within the lung on the same (ipsilateral) side as the primary tumor;
- N2, lymph nodes in the mediastinum on the same (ipsilateral) side as the primary tumor;
- N3, mediastinal or hilar lymph nodes on the contralateral side or beyond the mediastinal pleural envelope, which would include involvement of scalene or supraclavicular nodes on either side.

These designations reflect the prognostic significance of the pattern of lymph node involvement—lung cancers tend to affect nearby nodes in the lung first, followed by nodes in the mediastinum on the affected side. Migration of disease across the mediastinum or to more distant nodes is considered a significant advance.

The American Thoracic Society uses a mapping system that defines the anatomical boundaries of 14 lymph node stations—five inside the lung and nine mediastinal stations. Lymph node involvement in more than one station is considered significant.

M classification refers to metastatic spread to distant sites. In the case of NSCLC, M1 disease would include spread to the contralateral lung, lymph nodes beyond the regional stations, or other organs.

These refinements result in considerable heterogeneity of patient presentation within a given stage of NSCLC. Stage IIIA NSCLC is designated as T1–4, N0–2, M0.

A revision of lung cancer staging effective in January 2010 resulted in the upstaging or downstaging of several NSCLC categories. One important change was the reclassification of multiple tumor nodules in the same lobe from T4 to T3 and in different lobes of the same lung from M1 to T4. Malignant pericardial and pleural effusions, previously considered T4, are now designated M1a, as are tumor nodules in the contralateral lung. M1b is now the designation for distant metastases in this disease. ■



Understanding Cancer Risk and Risk Factors

Your risk factors might affect your need for cancer screening

We often hear that certain foods, such as processed meats, or activities, such as using a tanning bed, can increase people's risk of getting cancer. What isn't always clear is how these risks are determined and how substances, behaviors, and personal characteristics come to be thought of as "risk factors."

Risk factors

Risk factors are the characteristics and behaviors that can increase people's chances of getting cancer. There are four types of risk factors:

- **Behavioral** risk factors are behaviors or habits such as smoking, drinking alcohol, not exercising regularly, or not eating healthy foods.
- **Biological** risk factors are physical traits such as race, age, and sex.
- **Genetic** risk factors are specific gene mutations that people inherit from their parents. A person might have a genetic risk factor if he or she had several family members with the same type of cancer.
- **Environmental** risk factors are found in our surroundings, such as secondhand smoke, pollution, and pesticides. Viruses such as hepatitis B and C and the human papillomavirus (HPV) also are considered environmental risk factors.

What is risk?

When thinking of cancer specifically, "risk" is the chance of getting cancer for members of a particular group. The two types of risk are absolute risk and relative risk.

Absolute risk is the number of people who will be diagnosed with a type



of cancer in a particular time period—for example, in the United States, about 120 of every 1,000 women will be diagnosed with breast cancer in their lifetime. The absolute risk of breast cancer for women in the United States is thus 12%.

Relative risk is a comparison of one group's risk of getting a type of cancer to another group's risk. The risk for each group is calculated using data from clinical trials or from agencies like the National Cancer Institute that keep track of cancer statistics. The groups could be assigned according to sex, age, or some other characteristic.

A relative risk of 1.0 means the risk of developing cancer is the same for both groups—in other words, the characteristic being studied is not a risk factor for cancer. A relative risk below 1.0 means people with the characteristic are less likely to get cancer than are those without the characteristic. In contrast, a relative risk above 1.0 means people with the characteristic have a greater risk of getting cancer than do those without the characteristic.

For example, if the relative risk for lung cancer is 20 for a group of smokers compared with a group of nonsmokers, we can conclude that smokers, as a group, are 20 times more likely to get lung cancer than nonsmokers. We can also conclude that smoking is a behav-

ioral risk factor for lung cancer.

If the relative risk for colorectal cancer is 2.3 for a group of people with more than one first-degree relative (parent, brother, sister, or child) who had colorectal cancer compared with

a group whose first-degree relatives did not have colorectal cancer, we can conclude that people in the first group are 2.3 times more likely to get colorectal cancer.

Risk factors and screening

It's important to remember that these numbers don't reflect any one person's individual risk. Nevertheless, it's important to be aware of the risk factors that might place you in a high-risk group for getting any type of cancer.

For example, keep note of your family's cancer history, and keep your doctor informed of any changes in this history. This risk factor may affect your need to be screened for particular types of cancer. Likewise, being aware of behavioral or environmental risk factors, such as smoking or exposure to secondhand smoke, could help you avoid them. And people with exposure to environmental risk factors may be offered additional screening, such as low-dose computed tomography scans for people with a significant smoking history. ■

— M. Wade

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Compass

[Continued from page 6]

histological subtypes,” Dr. Tsao said. This further underscores the need for preoperative pathological analysis, which should include the status of tumor biomarkers, such as epidermal growth factor receptor mutation and the *EML4-ALK* translocation, as specific mutations in these molecular pathways respond differently to specific novel drugs.

Future directions

According to Dr. Tsao, a new clinical trial being planned at MD Anderson for stage III NSCLC will be a triple-modality trial in which treatment is tailored to the individual based on response to initial therapy. Treatment will include proton therapy and chemotherapy specific to histology, followed by either surgery or more chemoradiation. “The arms of this trial will be unique because they will be individualized,” Dr. Tsao said. “We are trying to push the envelope.”

The need for more individualized approaches to treatment will likely continue to be the driving force behind research initiatives.

A second trial will focus on patients with stage III NSCLC whose disease does not respond to chemoradiation or who have residual disease after chemoradiation. The goal is to determine whether additional chemotherapy or chemoradiation will help. “The 5-year overall survival rate among stage III NSCLC pa-

tients is 25%–30%,” Dr. Tsao said, “so we are trying to find additional treatments for them—we are still pursuing a possible cure.”

Two trials are in progress for patients with local-regionally advanced NSCLC whose performance status precludes surgery or conventional chemotherapies. One of these trials uses radiation therapy and celecoxib, and the other uses stereotactic radiation therapy. Patients with limited stage IV disease are included in the latter trial. “We are still committed to finding curative outcomes for our patients,” Dr. Tsao said, “even in the presence of advanced disease or inability to tolerate conventional treatments.” ■

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