

Yale CANCER
CENTER
answers

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An Update on Lung Cancer

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Yale Cancer Center Answers

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I am Bruce Barber and this is Yale Cancer Center Answers with Drs. Ed Chu and Ken Miller. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and an internationally known expert on colorectal cancer. Dr. Miller is a Medical Oncologist and the Director of the Connecticut Challenge Survivorship Clinic. Ken specializes in pain and palliative care. If you have a question that you would like to submit about cancer, please e-mail us at canceranswers@yale.edu or you can call 1-888-234-4YCC. If you are interested in listening to past editions of Yale Cancer Center Answers, each segment is posted on the Yale Cancer Center website at yalecancercenter.org. This evening, Ken cannot be with us but Ed Chu talks about the detection and treatment of lung cancer with Dr. Scott Gettinger and Dr. Roy Decker.

Chu Scott, let us start off by telling our listeners what lung cancer is and how common it is.

Gettinger Lung cancer is a common malignancy. It affects a little over 200,000 people in the United States annually. It affects men, women, smokers and nonsmokers. It is a disease primarily of the elderly, but we do see it in younger patients; I have patients in their 30s with lung cancer. Although it is not the most common cancer, it is the leading cause of cancer death in the United States. In fact, if you combine the deaths from breast cancer, prostate cancer and colon cancer, they do not equal the amount of deaths from lung cancer in a year.

Chu And what age group are we typically talking about for patients with lung cancer?

Gettinger Fifty percent of patients are over the age of 65; the median age is 70 years.

Chu What are some of the common symptoms that patients with lung cancer present with?

Decker Generally patients present with symptoms due to the progression of disease in their chest. This can cause difficulty breathing and, unfortunately, the disease tends to spread throughout the body before diagnosis. Patients present with all over body symptoms such as tiredness, fatigue, weight loss, and really just a failure to thrive.

Chu What are some common risk factors for developing lung cancer?

Decker Primary risk factor is smoking. There are other risk factors however. Radon is a gas that exists in the air and can accumulate in different structures, but primarily in basements, and we believe this can lead to lung cancer. Asbestos is more of a risk factor for mesothelioma, but with smoking it increases your risk of lung cancer.

Chu So smoking by far is the number one risk factor?

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Decker Yes.

Chu Is there any truth to the fact that if someone stops smoking, they can completely eliminate the risk of developing lung cancer down the road?

Decker No, but if you do not smoke the risk of you developing lung cancer goes down substantially. The more years out you are, the less chance you have of developing it, but you will always have a higher risk than the general population.

Chu Roy, what do we know about the issue of second hand smoke leading to lung cancer, which we hear a lot about in newspaper reports?

Decker Well it does seem that significant exposure to second hand smoke causes people to develop some of the same metabolites as smokers. We think it does put them at risk for lung cancer. It is always difficult to tell, certainly smokers have a higher risk, but we do feel that environmental exposure to smoke also puts you at risk for lung cancer.

Chu What is known about the genetics of lung cancer? If there is a family history of lung cancer, does that increase the risk for a family member of developing lung cancer down the road?

Gettinger There is definitely a family component and patients can have a history of not only lung cancer, but other cancers as well. We are beginning to learn a little bit about the molecular underpinnings of lung cancer. Here at Yale, we are specifically looking into this and have designed a trial where we are looking for patients at high risk; part of that risk assessment is family history.

Chu And what are some of the specific genes that are being looked at?

Gettinger EGFR mutations, which occur in maybe 10%-15% of the patients; this is an important pathway for cancer. It is called the epidermal growth factor receptor pathway and we actually have targeted therapies that treat this patient population.

Chu So if someone feels short of breath, is coughing a lot, has chest discomfort, malaise and fatigue, what should they do next? Who should they go see and how should they get things evaluated?

Decker I think everything should start with their primary care doctor. A lot of these patients, being long-term smokers, do have other pulmonary problems and so many are followed up by pulmonologists, lung specialists. The cause of those kinds of symptoms in someone who is a smoker is not always lung cancer. There are certainly a lot of other benign reasons that can cause those kinds of symptoms so they do need a thorough evaluation.

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- Chu Are there special x-rays that would need to be done to further evaluate?
- Decker Typically, an evaluation would start with a chest x-ray and most of those patients would be followed up with a CT scan of the chest. There has been some interest in screening lung cancer patients with CT scans, but it has not yet been shown to impact quality of life for the survival of patients with lung cancer.
- Chu As I understand there have been some mixed reports that we have been hearing. Some say that screening with the high resolution CT may be beneficial, some say it is not. Maybe we can get both of your views as to the potential role for CT scanning.
- Gettinger There were two studies done recently that have been presented in major medical journals. The first trial presented suggested that there was potential survival advantage in screening patients who have a high risk of lung cancer. However, a subsequent trial which was presented within the last few months suggests that there is no survival advantage and the only thing that CT screening does is find tumors earlier; that does not necessarily translate into survival advantage for many different reasons. One reason is that the nodules or tumors that they find might be benign and never cause a problem. So even if you do detect them, it is not necessarily going to improve survival. CT screening can be potentially problematic because in a majority of patients you find some abnormality and then the question is, what do you do with that abnormality? Do you biopsy it? Do you follow it with CAT scans? Once you tell a patient there is a shadow on their lung, the patient obviously will have some psychological stress and will have to wait until the next CAT scan. These patients sometimes have biopsies which are really not necessary and that can cause problems and complications. Right now, our feeling here at Yale is that there is no role yet for a CT screening in high risk patients, although patients are encouraged to enroll in clinical trials looking at this. Presently, there are two major clinical trials looking at this. The one in the United States is comparing screening with CTs versus screening with x-rays in patients. We already know that x-rays do not improve survival in terms of patients who are diagnosed with lung cancer at an earlier stage.
- Chu But also x-rays are not sensitive enough to pick up lesions relative to CAT scans.
- Gettinger Definitely. CT scanning picks up many more early stage lung cancers, however, we do not know if that will translate into improved survival in the population.
- Chu We have an e-mail from Timothy who says, "I am a 56-year-old male and smoked for 10 years when I was younger. Is there a way to improve my health and further decrease the risk of developing lung cancer?"

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- Gettinger This is a very common question that we get from both our patients who have completed treatment, and from their family members who are obviously thinking about reducing their own risk. The most important thing to do is to encourage these patients to continue not to smoke and limit any other exposure they may have. There have been many trials on what we call chemoprevention for lung cancer. This is trying to prevent lung cancer in patients just like Timothy. These have been conducted over in Finland and in the United States. As of yet, they have not found that the addition of routine vitamins or other nutritional supplements prevent lung cancer. In fact in some trials, it has seemed to increase the incidence of lung cancer. At this point I do not feel that any firm recommendation can be made for supplement use. My recommendation is usually to encourage the patient to continue not to smoke, and in terms of reducing the risk of other cancers, try to follow a low-fat, high-fiber diet.
- Chu Any other lifestyle changes that you can recommend to Timothy and our listeners out there?
- Gettinger Other than not smoking and trying to avoid places where there is a lot of smoke, for example if a family member smokes hopefully they can smoke outside, routine follow ups with your physician and health maintenance. Otherwise there is nothing else that we can recommend at this time.
- Chu Many folks out there believe that patients diagnosed with lung cancer have poor outcomes by and large. What are your thoughts on that? Is that truth or myth?
- Gettinger That is a myth. The majority of patients who present with early stage disease are cured of their cancers, usually with surgery and possibly with chemotherapy. We can cure a good amount of patients with more advanced, what we call locally advanced disease; maybe one in four of them. With newer therapies and supportive treatments, even patients who have metastatic disease are living well over a year with good quality of life. I definitely think that people can do well once they have a diagnosis of lung cancer.
- Chu How do you approach patients with early stage and more advanced stages of lung cancer here at Yale Cancer Center?
- Decker The most important part of the evaluation of a patient with lung cancer is a multidisciplinary approach. We are very lucky to work with Dr. Frank Detterbeck who is a famous thoracic surgeon here at Yale. All of our patients undergo a thorough evaluation and meet with Dr. Gettinger, who specializes in chemotherapy for lung cancer, and one of our radiation oncologists, a thoracic surgeon and a pulmonologist. We have a lot of imaging available here, and it is relatively routine to obtain CT scans, PET scans and MRIs. Additionally, I think every patient has to be evaluated for their underlying pulmonary disease. Many

of these patients have difficulty with breathing, and that is really going to impact treatment choices down the line. When we have gone through that, we get together as a group and discuss what we feel would be the best approach for treating the patient; whether that be surgery, chemotherapy, radiation, or some combination.

Chu Great. We would like to remind you to e-mail your questions to canceranswers@yale.edu or call 1-888-234-4YCC. At this time, we are going to take a short break for medical minute. Please stay tuned to learn more information about lung cancer and the latest advances in treatment of lung cancer with our special guests Dr. Scott Gettinger and Dr. Roy Decker from the Yale Cancer Center.

Medical Minute

The American Cancer Society estimates that in 2007, over 11,000 people will be diagnosed with colorectal cancer in Connecticut alone. Early detection is the key. When detected early, colorectal cancer is easily treated and highly curable. Men and women over the age of 50 should have regular colonoscopies to screen for this disease. Patients with colorectal cancer have more hope than ever before. Each day, more patients are surviving this disease due to increased access to advanced therapies and specialized care. New treatment options and surgical techniques are giving colorectal cancer survivors more hope than they have ever had before. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for colorectal cancer. Patients enrolled in these trials are given access to medicines not yet approved by the Food and Drug Administration. This has been a medical minute. More information is available at yalecancercenter.org.

Chu Welcome back to Yale Cancer Center Answers. This is Dr. Ed Chu and I am here in the studio with my special guest experts, Dr. Scott Gettinger and Dr. Roy Decker, discussing the latest treatment options for patients with lung cancer. Before the break we were talking with Dr. Decker about the multidisciplinary clinic here at the Yale Cancer Center. Again, for our listeners out there, both Drs. Gettinger and Decker are part of the thoracic oncology program, which I think has developed the multidisciplinary clinic approach to the greatest extent of all the different disease teams that we have here at the Yale Cancer Center. When a patient is evaluated and reviewed by your TOP program, as you call it, how are the decisions made as to whether or not a patient undergoes surgery, chemotherapy and radiation therapy?

Gettinger All new patients who present to the Yale Cancer Center, whether they present to a

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pulmonologist, a surgeon or a medical oncologist, are evaluated in one of our tumor boards where we all get together and look at their pathology slides and their imaging studies. In the room we have radiation oncologists, surgeons, thoracic surgeons, pulmonologists, pathologists, radiologists, social workers and a host of other individuals. Together we make a decision as to what the diagnosis is, what stage the patient is in, and what the best treatment modality is. In this situation more heads are better. We clearly have changed our decisions based on the input from a pathologist or a radiologist and it is very helpful. I think this is what is lacking in the community where they see a lot of patients with many different types of malignancies, but here at Yale in the thoracic program, what we see every day is lung cancer. We are more aware of the new answers for it.

Chu When would we typically consider surgery as the main modality of treatment?

Gettinger As you asked earlier in terms of what the different stages of lung cancer are, there are three general groupings of lung cancer. There are actually four stages, but I look at it as three different groups. The first group is early stage lung cancer. What that means is that your tumor is limited to either the lung or to the lymph nodes within the lung, and these are patients with stage I and II disease. The goal of treatment with these patients is cure. The way we do that is surgery, possibly followed by chemotherapy, depending on the characteristics of the tumor and of the radiographs. The next grouping is locally advanced disease which most often means that you have lymph nodes in the center of your chest outside the lung, but not in distant sites. We treat these patients for cure as well. The way we treat them is with combination chemotherapy and radiotherapy. It is a very aggressive approach, but again the goal of this therapy is cure, and we do cure one in four patients depending on the situation. The role of surgery in this group of patients is unclear but we do have a clinical trial investigating trimodality therapy; meaning chemotherapy, radiation, and surgery. Again this is a very aggressive approach for a patient who is able to tolerate it. The final grouping is metastatic disease. The goal of treatment with these patients is palliation; improve survival, but more importantly improve quality of life and symptoms. We do much better than we did say 5-10 years ago with this. We generally use chemotherapy and other supportive measures such as radiotherapy.

Chu Picking up on radiotherapy, Roy, when do you come in and say that radiation therapy really has a key role to play in treating patients with lung cancer?

Decker There are two main roles for radiation in the curative treatment of lung cancer. The mainstay is in patients with what we call locally advanced disease that has spread to the lymph nodes in the middle of their chest. The basis of their treatment is going to be radiation in combination with chemotherapy. Advances in imaging and treatment applying to radiation have made possible many strides in

that area to reduce the toxicity of the treatment and to increase its efficacy. Something that we are very excited about at Yale is the role of radiation in early lung cancer. It is important to say that the mainstay of treatment for early lung cancer is always going to be surgery, but there are a substantial number of patients who are unable to undergo even a minimally invasive surgery for a relatively small lung cancer. We now have a technique that we call body radiosurgery that allows us to treat these tumors with very, very high doses of radiation over only three or four treatment sessions. So a treatment that used to take seven weeks and involve significant side effects, can now be done in one week with minimal side effects. The bonus is that it works far, far better than our traditional techniques and in fact, it is being compared in randomized trials to surgery in Japan, and they are talking about doing that in this country as well.

Chu So this technique of radiosurgery would be used for patients who are not good candidates for surgery?

Decker I think at this point, it would be the standard of care for patients who are not candidates for surgery. Although I have to say, this is where it is vitally important to have a multidisciplinary approach because there are new surgical techniques available. There is minimally invasive thoracic surgery where it is really important to get your thoracic surgeon, your medical oncologist, your radiation oncologist and your pulmonologist all in the same room discussing what they can offer a patient and what the potential drawbacks would be of each approach.

Chu Roy, is there any role for radiation therapy once surgical removal of the lung cancer has been done?

Decker Yes and this is an area of some controversy. But there is good evidence that when patients have lymph nodes that have spread to the middle of their chest, what we call the mediastinum, they benefit from radiation after surgery. This is based on several studies, one of which was pioneered here at Yale looking at outcomes of patients who were treated with radiation following surgery. We tend to evaluate these patients on a case-by-case basis. Many of them we treat with radiation and chemotherapy before surgery. We also have the option of treating them after surgery.

Chu And what are some of the side effects that patients might experience if they in fact receive radiation therapy?

Decker Standard radiation involves treatment of not only the tumor, but the surrounding lung tissue as well as other normal structures in the middle of the chest like the esophagus. During treatment the esophagus tends to be the cause of most of the trouble. Patients have a lot of problems with pain while swallowing and can

require pain mediations. What we worry most about is the treatment of the normal lung tissue because the radiation will destroy normal lung tissue that surrounds the tumor. If we are not meticulous about our radiation treatment planning, we can leave the patients more short of breath than when we started. That is the advantage of some of the new techniques that we use; we are able to treat less normal tissue while getting a larger dose into the tumor.

Chu Scott, turning to chemotherapy, I think one of the significant advances just over the last few years has been the development of targeted therapies. Can you explain for listeners what that means, especially as it relates to the treatment of lung cancer.

Gettinger The targeted therapy means different things to different folks. Chemotherapy is targeted in a sense, but it is not very specific. Chemotherapy affects primarily DNA, or something called the mitotic apparatus, and it affects anything that grows quickly in the body. You have many of the side effects that people are concerned about with chemotherapy. Targeted therapy takes advantage of our knowledge of molecular biology and what is going on at a genetic level, and also at a protein level in the cancer. Taking advantage of that knowledge, we design therapies that are specifically targeted against that tumor rather than just general things that happen in any cells that divide quickly.

In lung cancer there are two so called targeted therapies which are presently used. They are FDA approved and one of them is called Tarceva. Tarceva is a molecule that interferes with the EGFR (epidermal growth factor receptor). We talked about this a little bit earlier. This is a very important pathway in cancer and in some patients there is mutation, and in other patients it is overexpressed. This drug Tarceva, which is a pill, has been shown to improve survival in patients with lung cancer. The other targeted therapy we have is called Avastin, which is the monoclonal antibody to a molecule that runs in the blood called vascular endothelial growth factor. This is very important in promoting new blood vessel growth. The way a tumor grows is it is fed, and the way it is fed is through the blood. If we can shut off the blood supply to a tumor, we can have positive effects in terms of treating patients with cancer. These are two of the agents that we presently use in lung cancer and we are beginning to combine both; preliminary results look very encouraging.

Chu In fact, you are hoping to open up a study here in the not too distant future, looking at the combination of antiangiogenesis strategy and anti-EGFR strategies correct?

Gettinger Yeah, it is going to be for the locally advanced group of patients. We are going to be using Avastin with chemotherapy to start, and then with the radiotherapy we are going to use Avastin, Tarceva and chemotherapy. Then after finishing curative

intent chemoradiotherapy, we are going to continue patients on the combination of Tarceva and Avastin, the two targeted agents that we have.

Chu That sounds like a pretty aggressive but very innovative approach to try and treat patients with lung cancer.

Gettinger We are very hopeful about this combination.

Chu Any other clinical trials you are working on that you would like to tell our listeners about?

Decker We have plenty of clinical trials here at Yale for lung cancer in different types of categories. We have some lung specific trials. For example, for small cell lung cancer we have a trial of a novel agent called cloretazine. For non-small cell lung cancer, we already have a protocol for the locally advanced patients. We have other trials which we call phase-I trials, that we are offering to our lung cancer patients. These can all be found at the Yale Cancer Center site listed under either lung solid tumors or phase-I trials.

Chu I would like to thank Drs. Gettinger and Decker for a terrific session this evening on Yale Cancer Center Answers. Until next week, this is Dr. Ed Chu and my co-host Dr. Ken Miller who is out this week, from the Yale Cancer Center, wishing you a safe and healthy week.

If you have questions, comments, or would like to subscribe to our Podcast, go to yalecancercenter.org where you will also find past broadcasts in written form. Next week, we will examine the role that genetic testing can play on our healthcare with Ellen Matloff. She is a research scientist and the Director at the Yale Cancer Center Genetic Counseling Program.