

Advances in the Treatment of Lung Cancer
Webcast
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Dr. Jyoti Patel

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Andrew:

This is Andrew Schorr with Patient Power and welcome back to another one of our biweekly webcasts on nmh.org in the HealthNet section, where we connect you with leading Northwestern experts on important health topics. And one of the ones we've been covering lately is lung cancer which, unfortunately, is an all-too-common cancer and all too often is fatal. But we're making progress. So this is really our series now is to help you connect with the latest information and leading Northwestern experts to understand where we are and how you can get the best care for you or someone you love.

Just a couple of weeks ago we did a program with Matthew Blum, who is a lung cancer surgical specialist and also leads the multidisciplinary team there. He explained surgical approaches. Today we have as a guest Dr. Jyoti Patel, who is a medical oncologist. She's an assistant professor of Medicine in the Division of Hematology/Oncology at the Feinberg School of Medicine at Northwestern University. She's a member of the Robert H. Lurie Comprehensive Cancer Center and is certainly one of the leading thoracic oncologists in the country and is one you can see at Northwestern Memorial Hospital.

Dr. Patel, welcome to the program.

Dr. Patel:

Thank you so much.

Andrew:

So when we think about drug therapy to help people with lung cancer, certainly there's surgery often and there's radiation. Where does drug therapy come in? And have your tools that you have been expanding lately?

Dr. Patel:

We have made tremendous strides in the treatment of lung cancer, particularly in drug therapy, in the past several years. Remember that of the over 200,000 Americans who will be diagnosed with lung cancer in 2007 the vast majority of them will be treated with chemotherapy at some point in their therapy. A minority of patients have disease that is initially resectable by surgery. About a third of patients have disease that is in the center of their chest, or locally advanced disease, for whom we usually do combination chemotherapy and radiation or combination chemotherapy and surgery. But about 50 percent of people will have

disease that is metastatic or advanced or stage IV at the time of diagnosis, and chemotherapy is really the backbone of their treatment. The therapy is certainly to make their lives longer but substantially to increase or improve the quality of their lives and decrease lung cancer-related symptoms.

Andrew:

Now, you mentioned that things are changing. So what's changed in the last few years? You know, it used to be a pretty bleak diagnosis. It's certainly a very serious one no matter what, but it sounds like you have more tools now. And they continue to change. And maybe you could also help us understand as you have these tools how you understand which patient they're right for.

Dr. Patel:

The time line for chemotherapy in lung cancer is pretty short. And as late as the early 1980s we had one or two drugs, and most of our treatments were related to either decreasing pain or improving breathing with things like steroids. In the 1990s there were multiple new chemotherapy drugs that were approved, and most of these drugs were very tolerable and consistently improved survival.

Since 2000 though, we finally have a better grasp on what makes lung cancer grow. We understand that there are molecular aberrations or overexpression of certain proteins that cause a cancer cell to divide and become invasive and find a way into the bloodstream and to resist programmed cellular death. So we use some of these new targets to help us find drugs.

The pharmaceutical industry in recent years has developed molecular drugs. One class of them are the EGFR tyrosine kinase inhibitors. This is an epithelial growth factor inhibitor. And this is a protein that is overexpressed on cancer cells, particularly on lung cancer cells and not so much on normal cells. This protein transverses the cell membrane of a cancer cell, and part of it is on the outside of the cell and then there's a workhorse element on the inside of the cell.

That element on the inside of the cell is called the tyrosine kinase, and it is a protein that turns out cellular signals causing cancer cells to grow. The extracellular part generally responds to signals from the rest of the body. So either other cells are sending proteins that are activating this EGFR tyrosine kinase. And when that signal occurs there's activation on the inside of the cell.

What we found is that we can block this activation with some of these new medications. So drugs like Tarceva and Iressa are pills that you can take orally every day, and they're swallowed, rapidly absorbed, and they go to these cancer cells that express these proteins, and they shut these proteins off and cause the cells to stop replicating and sometimes to die.

Andrew:

Let me just kind of spit this back to you a little bit to see if I understand. So I imagine there's this sort of party line of communication between cells, cancer cells and others. And so now you have, you mentioned, a couple of these drugs to kind of cut the wires of the party line, stop that communication, stop that messaging for cancer cells to divide and grow.

Dr. Patel:

That's absolutely right. Some of these new drugs are easy to take. The nice part about them is that they target cancer cells. They only affect the cancer cells. They don't cause the side effects that traditional chemotherapy used to cause. They don't affect your bone marrow. They don't cause you to lose your hair, for example. They don't affect your nerve endings. You get to take them at home with a glass of water. And we've seen people who've been on these drugs for a prolonged time without significant problems.

Andrew:

Let me add one other drug. One drug, if people do research they've also heard of this one called Avastin. Where does that come in for lung cancer?

Dr. Patel:

Avastin is a drug that was approved for lung cancer in November 2006. It has been used for colon cancer and breast cancer for some time before that, and has only had FDA approval for colon cancer prior to lung cancer.

Avastin is a drug that is the end of many years of research into angiogenesis. If you recall Judah Folkman and others early on described that cancer cells could cause blood vessels to grow and to basically feed the tumor. Our hope has been for some time now to cut off the blood supply. If we can cause blood vessels to normalize and sort of strangulate the tumor we can see improved responses.

Avastin is an antibody. It's a protein that blocks tumor cells from secreting those signals that cause blood vessels to grow. And it's given by vein periodically, once every two weeks, once every three weeks, depending on what kind of tumor you have. And what we've found is when we give it in combination with chemotherapy we see astounding results. We see that tumors shrink more quickly. We improve the rates of response. We also have noted that people live longer when they've received Avastin compared to standard chemotherapy alone. So in 2006 it was approved in combination with chemotherapy for patients with advanced lung cancer.

Now, it too is a targeted drug that affects the protein and not so much normal cells like your blood lines or your hair. It doesn't cause a lot of nausea. But we use it with some trepidation in certain patients. We find that in patients with squamous cell lung cancer that we have to use it very carefully or not at all. Currently it's not

indicated for patients with squamous cell lung cancer, because it may cause these patients to bleed. We use it only in patients with nonsquamous, non-small cell lung cancer.

Andrew:

Now, that goes to another question. So you have these new drugs, these new tools to use with or without chemotherapy or in whatever combination you feel is right. When we use this term molecular profiling to understand, well, what's the specific lung cancer situation for a patient who needs drug therapy, how do you do that? And then how do you decide which is right for which patient?

Dr. Patel:

For years when a patient was diagnosed with metastatic lung cancer we gave one of a couple of drugs for a prescribed amount of time. Recently we've made considerable advances not only in terms of how many drugs we have but in also predicting which patients will respond to particular drugs. Tumor cells acquire mutations as cancers grow. And so that means that their DNA has changed, and we can sometimes pick these mutations and predict who will respond to a certain therapy.

In some patients who were treated with Tarceva or Iressa early on we recognized that a fraction of patients seemed exquisitely sensitive to these drugs. And clinically we said, Oh, these are primarily patients with adenocarcinoma or bronchoalveolar carcinoma. They tended to be Asians. More of them were women than men, and many of them had less of a smoking history. So we had these clinical parameters, but then we looked a little further and found that patients who had a particular mutation in their DNA were the ones who were the most sensitive to these drugs. This mutation made these drugs bind tighter to the protein that we were try to go shut off.

Now we can take a tumor specimen sequence for this DNA to see if someone harbors that mutation, and if they do they're very likely to benefit from these newer targeted agents.

Other groups have looked at trying to get a DNA signature of five or ten genes when mutated that can predict whether patients will have more or less aggressive disease. So if someone, for example, has undergone surgery as part of their therapy for stage I or stage II cancer our hope would be that eventually we will be able to take the tumor, we'll be able to sequence the DNA and predict the likelihood for that individual that the cancer will come back. If they have a high chance of the cancer coming back we'd want to treat them with chemotherapy to reduce that risk. If they were destined to be cured from the surgery alone then we'd like to save them the toxicities of chemotherapy.

Andrew:

Yeah, it's fascinating, and the science is moving forward, which is encouraging. Let me ask you about the whole idea of surgery and chemotherapy. So now sometimes you do drug therapy before surgery, and then other times you're recommending doing it afterwards. So tell us about the sort of before surgery, the neoadjuvant part of it, I believe, trying to shrink the tumors so that the surgeon has sort of a more localized area to go after, and then this whole idea of adjuvant therapy afterwards.

Dr. Patel:

So for many years we believed that surgery alone was the best curative option for patients with early stage disease. There was no compelling benefit in the 1990s and 1980s that we could improve survival by giving chemotherapy around surgery. There were multiple studies, though, in this century that sought to use some of these newer, more effective drugs to improve the landscape. One such method was to give induction or neoadjuvant therapy, and the idea was that you could make an easier target for a surgeon.

For oncologists that also meant that we were more likely to get the drug into a patient. As you can imagine after surgery sometimes the tolerance for chemotherapy is decreased. So there were a few studies looking at whether we could give chemotherapy before surgery. And there were two trials in the 1990s that compared surgery versus chemotherapy before surgery, and the outcomes of chemotherapy before surgery were better.

And it was felt that patients who had big burden of disease, so their primary tumor was enlarged or lymph nodes were enlarged in the center of their chest, that we could give chemotherapy. And we use a term called downstaging, meaning that we take them from having more advanced disease to having less disease, so we'd bring them down to stage I perhaps. And if we could do that we would benefit the patient.

At the same time as this many investigators were looking at chemotherapy after surgery, or adjuvant chemotherapy. And a couple of trials have been reported in the past several years that show that we can consistently improve survival with chemotherapy after surgery, particularly in stage II and III disease. So with the current landscape we tend to give chemotherapy after surgery, because we have multiple large randomized trials that suggest a survival benefit.

There are those of us who still like to believe the idea of induction chemotherapy, and we recommend that for patients with bulkier disease. If they have a nice reduction in their tumor load, then we would suggest surgery. But by and large in 2007 adjuvant chemotherapy, or chemotherapy after surgery, is the preferred option unless you're on a clinical trial.

Andrew:

Thanks for explaining that, Dr. Patel. Now, so people look at the overall statistics, and these studies come out, whether from your big ASCO meeting, American Society of Clinical Oncology, which was recent, or any time during the year, and they hear the statistics, and overall in lung cancer they're not great. There are other cancers where the statistics are looking brighter, but there is progress being made. Somebody comes to see you as an individual and they're weighed down by those statistics. What do you tell people on how they can begin to understand what is their lung cancer situation, what are their options, and give them hope for moving forward?

Dr. Patel:

I think statistics for lung cancer are incredibly misleading. You have to realize that we're talking about 200,000 individuals annually, and it's a pretty heterogeneous group. We have patients who are in their 30s who have never smoked who have no other medical problems who have lung cancer. We group them with patients who are in their 90s with heart disease and diabetes when we report statistics.

For the individual I think it's very different. When we talk about average time we mean that 50 percent of people do better than a particular number and 50 percent of people do worse. You need to make sure that you take in as many factors as possible -- What other medical problems does an individual have? What's the load of cancer that someone has? What is their intrinsic biology of their disease? -- before we make any summation.

The fact is, though, none of us are very good at predicting how long someone will live. If doctors were better at it they'd probably be on Wall Street. The idea is that we can give an estimation of a population of people, but for the individual it's black or white. Either you're doing well or you're not. You have to know also that although we have median survivals that seem that they haven't improved substantially in a decade, we know that higher and higher fractions of people are living two and three years now, which was essentially unheard of a decade ago.

The proportion of people living with their cancer and being very active in their lives, taking care of their families, working and being very present with few side effects from chemotherapy has grown substantially in recent years, and I think that is the biggest reason for optimism, the fact that in certain patients we can make this a chronic disease.

Andrew:

Yes, we've been discussing that in some cancers. So when you go for surgery hopefully it can be curative. And then where these other therapies come in, which may be radiation or your area of medical oncology, to have the therapy be targeted for you to keep the cancer at bay and then go on with your life hopefully for a long time. Did I state it correctly?

Dr. Patel:
Absolutely.

Andrew:

Okay. So therefore let's talk about what you offer at Northwestern, because you're a thoracic cancer specialist. You're a lung cancer specialist. We had on Dr. Blum. That's what he does from the surgical side. You have radiologists who specialize in lung cancer. You have radiation oncologists who specialize in lung cancer. That's not everywhere. And you getting together all the time, and you're talking about cases. So if--as we've heard from you, there's improvement, and there's studies and there are new resources coming together to treat lung cancer and understand specific sub types of lung cancer. It would seem to me that someone would do well to consult with a group like yours so say, Well, I may live out in the hinterland and, yes, there may be other hospitals, but at least have you look at my case, because after all it's life threatening and things are changing.

Tell me your take on it. Because you meet all the time to discuss cases, and you have people, patients who may need surgery, may need radiation, may need drug therapy, and you're a team talking together about those cases, right?

Dr. Patel:

Absolutely. I think the landscape has become much more complex in recent years as we have multiple new drugs, as we have some understanding of molecular biology. The number of trials that are presented annually at our national meeting has increased tenfold in two decades. It's very difficult to stay current with all the information. I think what coming to a comprehensive cancer center offers is that multidisciplinary aspect. We all speak frequently during the day. We discuss cases, and you have more than one person talking about your history, reviewing your films and your pathology and really talking about how to optimize your outcome.

I think also because of the volume of lung cancer we see we have some ability to know when it's time to really push the envelope and do things that could be a little bit unconventional to improve survival in certain individuals. I think that's very difficult to do when you are a solo practitioner.

Andrew:

Right. I was going to make that point. I think--I believe it so strongly, there's an art of medicine. And certainly oncology maybe originally was more that, what did you feel in your gut was right for a patient, and then we got all these clinical studies and then you have algorithms for what you do.

But now I think we're back. There's that art overlay, if you will, and that is that you have many tools, and there are different modalities that come together in cancer care, in lung cancer certainly. So it's really we're drawing upon the

experience of you and your colleagues to say what's right for me. And that's a valuable brain trust and a whole depth of experience that I'd want on my side.

Dr. Patel:

Thank you. I think one additional thing is that it is very difficult in today's world to get a new agent approved. So there are drugs that look very promising, but they are going through all the regulatory processes for several years before they're approved. Many of these drugs are still in clinical trials, and you can gain access to some of these novel agents by willingness to participate in a trial. Remember, they're trials, so we don't know if they're better than standard therapy, but certainly most of the drugs that are farther along in development have a bit of a track record and we can say, Oh, this might be a good option for you. So the access to novel agents at a comprehensive cancer center I think is very important.

Also in a comprehensive cancer center we tend to have all of the other modalities. We have a nutritionist, we have a psychologist, we have a social worker dealing with the holistic impact of a diagnosis of lung cancer on the individual as well as the caretaker, because I think your support system when you're dealing with a disease like this is key and having as many people on your side is pretty important.

Andrew:

I couldn't agree more, and that's what I did with my own leukemia is consult with specialists. And I was in a phase II clinical trial but at that point was at a single academic medical center. And so I understood. I signed a lot of papers. I knew it might not be more effective but I'd be monitored carefully. I understood the risks. As it worked out I did get tomorrow's medicine today. I would imagine for people with lung cancer in consultation with you and the rest of the team that would be--while we don't know all the answers, you're going to be watching them carefully and it could give them the chance of that.

I imagine when these drugs that you mentioned, Avastin, Tarceva, Iressa, others, when they were in trials there were patients who certainly benefited, led to the approval. Are there other agents like that now that might be appropriate for someone in a trial at Northwestern. That's an important discussion to have with you, I would imagine, Dr. Patel.

Dr. Patel:

Absolutely.

Andrew:

So, folks, if you're listening, no matter where you are in the world, and certainly in you're in Chicago land or even a drive down the freeway, I think you want to say, Have I been diagnosed with a cancer where it makes sense to have a consultation

at least with a team that's devoted to lung cancer. And in the case of Dr. Patel this is what she does as a medical oncologist. And fortunately, as we've heard, things are changing.

So, Dr. Patel, from where you sit are you encouraged? Obviously we'd want the train of better treatments to rush ever faster and for the word "cure" to be used much more often. But you've been at this a while and you have a long career ahead of you. Are you encouraged?

Dr. Patel:

Absolutely. There's a tremendous reason for optimism in 2007. We've come a long way, and we are just now really reaping the benefits of years of basic research. And we'll make that into clinical improvement for our patients.

Andrew:

So people wonder, do you invite questions from patients you know? I preach with Patient Power that knowledge is power and that it's really important for you and family members to get smarter and that they can work as a key part of the team with you as you try, hopefully, to have people live a long, healthier life. So for you, I mean, you're an eminent lung cancer specialist, do you welcome that dialogue?

Dr. Patel:

Absolutely. Patients are their best advocates, and it's important for me to be challenged when a patient tells me a new symptom or I need to figure out a way to treat their tumor more effectively. It's instructive for us all. But absolutely, I think taking an active part in your medical care, finding physicians that you feel most comfortable with who are giving you undivided attention I think is the key to a better outcome.

Andrew:

One other thing about drug therapy and that is we mentioned this word chemotherapy and, you know, people don't look forward to the side effects certainly of some of the drugs that have been around for a while, and we've talked about these new targeted therapies. But it sounds like some of what you're doing certainly on a daily basis is using drugs together. Chemotherapy is not dead, right? It has a place when appropriate with some of these more targeted therapies.

Dr. Patel:

Absolutely. We've been using them hand in hand currently. We're looking at other approaches, including vaccine therapy, other molecular targets. But still the backbone of therapy is chemotherapy. And chemotherapy in many senses is targeted. We know what cellular processes that traditional chemotherapy interrupts and kills cancer cells.

Andrew:

So one last area, and that is you teach in the medical school, the Feinberg School of Medicine. So when younger students are there and they say, Okay, Dr. Patel, where is this headed? What will the tools I will be using, you know, as I treat lung cancer patients. Look in your crystal ball, where we're headed.

Dr. Patel:

We will come to a day that we are able to check the serum or the blood or even a buccal swab, so the line of your cheek, for DNA that gives us tracks or insight into what the cancer's doing. We'll look for proteins that are expressed and tumors that are methylated to develop specific therapy for patients. We'll have a chemotherapy cocktail, so to speak, that would be individual for that patient. We're getting there. It just take a little while.

Andrew:

And of course this comes out of partnership between families, patients affected by lung cancer now to work with you in research so we get the answers we need to move things forward. And I know you welcome that when families and patients consider participating in trials.

Dr. Patel:

Absolutely. It's out of their generosity that they give us their serum samples or allow us to test their resected tumors for protein expression. For that we're most grateful, but that we think improves cancer care for all individuals.

Andrew:

Dr. Jyoti Patel, any final comment you'd like to make?

Dr. Patel:

We've come a long way in the past 20 years, particularly in the past five years, and we'll continue to make great strides. Lung cancer affects far too many Americans in 2007, and if we can decrease the burden on American health we'll do a service to all of us.

Andrew:

Well, we wish you well with all your work at Northwestern.

We've been visiting with Dr. Jyoti Patel who is assistant professor of medicine. She's in the division of hematology, oncology, Feinberg School of Medicine and at Northwestern university and of course sees patients at Northwestern Memorial Hospital, part of interdisciplinary team.

Dr. Patel, thank you so much for being with us on our Patient Power webcast on nmh.org in the HealthNet section and NMH's devotion to patient education.

Dr. Patel:

Thank you so very much for your time.

Andrew:

Thank you, ma'am.

And I just want to mention to our listeners, take a look at the replay of our interview earlier with Dr. Matthew Blum, who is a thoracic surgeon. And taken together, your understanding of surgery and certainly we've discussed along the way a little bit about radiation and where that comes in and I'm sure we'll do more, you'll have a very comprehensive understanding of today's treatment of lung cancer.

This is Andrew Schorr with Patient Power. Thanks to Northwestern Memorial Hospital for sponsoring our program and, as always, knowledge can be the best medicine of all. See you next time.

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