Personalizing Therapy for the Treatment of Patients with Lung Cancer

Webcast

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Ruth's Story

Andrew Schorr:
Lung cancer therapies tailored to a patient's individual disease are proving to be a more effective approach to treatment. Coming up, a specialist from Chicago's Northwestern Memorial Hospital explains the latest developments in targeted therapies and the benefits of multidisciplinary care, plus we'll meet a lung cancer patient who joins us to share her story. It's all next on Patient Power.

Hello and welcome to Patient Power sponsored by Northwestern Memorial Hospital. I'm Andrew Schorr.

Well, I think you know that our most common, the most deadly cancer, is lung cancer, and it is just way too common, unfortunately. It affects people who have never smoked as well as, of course, people who have smoked and smoked a lot or have been affected by secondhand smoke, and we're trying to do better in tailoring our therapy to exactly the type of lung cancer that a patient has to give them the best hope for a longer life.

I want to have you meet someone who has been dealing with that who wants to talk about her situation, and I think it's inspiring for others, and also meet her doctor at Northwestern Memorial, understand that she's part of a whole multidisciplinary team aimed at bringing a lot of modalities together to help people with lung cancer. We're going to learn about that during our program.

So let's meet Ruth Ashton. She lives right outside Chicago in Oak Park. She's 46 years old. She has two grown daughters, and they've given her three grandchildren with another one on the way. Ruth works at Loyola in the graduate school there. And, Ruth, you have a graduate degree yourself in sociology, right?

Ruth:
Actually, I'm working on it right now.

Andrew Schorr:
Okay. You've been studying that, and we're going to talk about how that's helped you along the way as you've learned about your own illness. But if we go back a couple of years, you're a runner, like me, four or five miles, which is great. Maybe you're not going to be in the Olympics, but you're staying in shape. Your health was always good, right?

Ruth:

It was indeed.

Andrew Schorr:
And maybe the worst thing that happened [to you] was kidney stones?

Ruth:
Right.

Andrew Schorr:
But you were having pain in your groin, and I know you had hernia surgery but they uncovered something else, didn't they? What was that?

Ruth:
They did. Well, I tried to start to run after my hernia surgery, and it was just impossible. It was too painful, and although I had tried to baby what I thought was an injury for a while it just wasn't going way, so I made an appointment with Dr. Sarah Edwards at Northwestern to see what the problem was. And she initially did an x-ray and found something suspicious. She thought it was a compression fracture, and she ordered an MRI, which then revealed that I had some sort of tumor. It wasn't [clear] what it was at that point.

Andrew Schorr:
Right. And this was sort of at the head of the bone, the femur that's part of the whole hip joint, right?

Ruth:
The femoral neck.

Andrew Schorr:
Oh, my. So that had to be just devastating. You feel you have a sports injury, and then you're told it's a cancer.

Ruth:
It was a shock. I think when you eat well and you exercise you kind of get implicit messages from society that you'll be okay, and so a cancer diagnosis was never on my radar at all.

Andrew Schorr:
Oh, my. So then the question is, well, what kind of cancer is it, and did it come from somewhere else. And as that was investigated, I know first they felt, well, given your age maybe it was breast cancer that had spread, but then shocker of shocker, it was lung cancer, right?

Ruth:
It was indeed.

Andrew Schorr:
And so this was I think what they call an adenocarcinoma, type of non-small cell

lung cancer, and so they found a spot on your lung, but they found some other spots around, too. Where were they?

Ruth:
I had a couple of good-size spots on my sacral, some on my spine, my brain and a small node in the liver.

Andrew Schorr:
And you had to go through a lot of workup at Northwestern to figure all this out, scans and even what they call VATS, a VATS procedure to go in and get tissue from the lung to analyze.

Ruth:
Right.

Andrew Schorr:
And then of course in early 2011 it was time for some drug therapy to try to shrink the tumors, so you began that. How has that combination therapy worked for you?

Ruth:
It's worked really well. I mean, initially I think the goal was to get me up and moving and maintain as normal of a life as I could, so they fixed the hip first. And then I was strong enough by the time I started chemotherapy to tolerate that well, and the effects have been phenomenal, in my mind.

Andrew Schorr:
Right.

Dr. Johnson:
Phenomenal from my point of view, too.

Andrew Schorr:
Okay. Let's say who that voice is, and that's Dr. Melissa Johnson, who is [Ruth's] medical oncologist and a lung cancer specialist, and Dr. Johnson, then, has been the quarterback, if you will, of these drug therapies coming into play and what would be right for Ruth's situation.

So let's continue with Dr. Johnson for a second. She's an assistant professor at Northwestern University's Feinberg School of Medicine. She's a thoracic oncologist, so she's a lung cancer medical oncologist, a specialist in that. So let's just get into that word, "phenomenal." So that's the trick, isn't it, to see what modalities and in this case drug therapies will work for which patient and when it's a win like this and it can knock the cancer back, as you say, it's phenomenal.

Dr. Johnson:
It is. I think the most important part about the combination of therapies that Ruth has been treated with is that they were targeted or tailored specifically to aspects of her tumor. So in particular we used the histology, or the way the cells looked

underneath the microscope, they were an adenocarcinoma, to select pemetrexed as one of the chemotherapy drugs that she would receive. And likewise we selected Avastin or bevacizumub as an additional agent based on her histology. We also included Zometa, which is a bone-strengthening drug because the cancer was found initially in the bones. And over all of the treatments that Ruth received, the cancer spots that we followed in the lungs as well as other places have shrunk considerably so that she has very minimal disease at this time.

Andrew Schorr:
And Ruth, we should mention, you've been back at work. You're back at the graduate school at Loyola, and you're working. You're home today with a cold, which any of us could get.

Ruth:
Yes.

Andrew Schorr:
But you're--you're moving on.

Ruth:
I am. I mean, I guess that's what you do. I mean, one foot in front of the other.

Andrew Schorr:
Well, we're going to talk more about how you wrap your head around this because I know with a serious illness like this people say I want to deal--I want to knock back the cancer, I want to beat it if I can, but I've got to work on my head at the same time, too, and your daughters, your husband, everybody, your grandchildren are concerned as well. So we'll talk about that along the way.

Understanding Non-Small Cell Lung Cancer

Andrew Schorr:
But let's get back to this whole personalized therapy idea, Dr. Johnson. Where are we now with lung cancer? I mentioned that she was diagnosed with non-small cell lung cancer, and we mentioned this term "adenocarcinoma." So first of all, help us understand, is non-small cell lung cancer the most common type?

Dr. Johnson:
That's correct. There are two major classifications of a lung cancer diagnosis, and it's mainly based on how the cells look underneath the microscope. There's small-cell lung cancer and non-small cell lung cancer. So for the purposes of our discussion today we'll leave small-cell lung cancer to the side because it is a different disease type and benefits from different types of treatment. But within non-small cell lung cancer we can further subdivide cancers, the lung cancer subtype into adenocarcinoma, which is the most common type of non-small cell lung cancer. Somewhere between 50 and 60 percent of non-small cell lung cancer diagnoses will be adenocarcinoma. The second type is squamous carcinoma, and about 30 percent of patients will have that diagnosis. And then another five to 10

percent will have a more rare histology, neuroendocrine or large-cell neuroendocrine carcinoma.

Andrew, you mentioned at the beginning and you were correct that smoking still remains the most common cause of lung cancer in the United States, but over the last decade many lung cancer specialists have come to recognize that there is a growing population of patients who are diagnosed with lung cancer that never smoked a cigarette, and these patients, like Ruth, are more likely to have the adenocarcinoma subtype.

Personalizing Therapy for Lung Cancer

Andrew Schorr:
As you're mentioning these different subtypes, it used to be in cancer, if somebody was diagnosed they'd say, "Well, where is it?" and we talked about how it had spread different places with Ruth, so staging was based on that. We didn't talk much about the biology. And then we have had the Human Genome Project identifying I think what you call oncogenes. How does all this come into play as far as tailoring therapy for an individual with lung cancer?

Dr. Johnson:
You're absolutely right. We've sort of drilled down on the lung cancer subtypes and asked what is it that makes a lung cancer develop in patients that are not smokers, that don't have that obvious causative exposure? And what we've found is that there are a number of genes, we call them oncogenes, that when they get turned on in a patient's, in a person's body can cause a cancer. And it's true across the board, not just for lung cancer that these oncogenes can be positive, but we have uncovered in the last decade and in particular in the last five years a number of oncogenes or mutations that are driving, we say, lung cancer development.

Andrew Schorr:
One step is to identify them, but then you [ask], "Well, what do we do about it?" Now, you mentioned Avastin along the way, that's one kind of drug. There are other drugs that have been developed, and so you may then choose drug A or B or C or even maybe a clinical trial, and we'll talk about those, too, for one patient and then a different group of drugs for another based on what you're learning. Tell us how that's working now and how your tools are changing.

Dr. Johnson:
You're right. I mean, you know, you're absolutely right. Its one thing to identify the mutation and it's another thing altogether to target that mutation with a therapy. I would say there are as many as 10 or 15 different oncogenes that we know play a role in lung cancer development, but there are two in particular for which therapies have been developed to block the activity of those mutations or oncogenes and thereby turn off the signal that's creating the lung cancer.

The two that I'm speaking of are a mutation first in the EGFR, EGFR mutations. EGFR stands for epidermal growth factor receptor, and mutations in EGFR occur in

about 10 to 15 percent of United States populations, closer to 20 to 30 percent in Asian populations. And mutations in EGFR can be treated with a therapy that turns off the signaling that results in a mutation in EGFR. We call the therapy that targets EGFR, erlotinib or gefitinib. Erlotinib, or Tarceva, is available in the United States, and gefitinib or Iressa is available mostly in Europe and Asia.

Andrew Schorr:
And then you have in the last few months or a year or so you have had something else.

Dr. Johnson:
Yes.

Andrew Schorr:
I know it's called an ALK inhibitor. What's that?

Dr. Johnson:
So there is a second oncogene that has been identified, and it's actually a fusion protein that results from two genes that get stuck together. EML4 and ALK are two genes that exist on chromosome 2. They are on separate places on chromosome 2, except in about five percent of lung cancer patients the two genes get smushed together through an abnormal cell division, and as a result the EML4-ALK fusion gene causes a lung cancer to form.

Now, that can also be targeted with a drug that turns off that fusion gene. It's called crizotinib or Xalkori. Now EML4-ALK fusion genes occur in a smaller number of patients in the United States, probably about five percent, but we also are finding that crizotinib is an effective therapy just recently, within the last year, FDA approved for this patient population.

The one other thing I wanted to mention about crizotinib is that fusion gene, that EML4-ALK, was only discovered in the laboratory in 2007, so here we are now five years later where we already have a drug that is making an impact in people as a result. Just to give you perspective, the average development of a targeted therapy can be on the order of 10 years, so the fact that we have been able to bring a target from the laboratory bench to the bedside, to the patient bedside we say, in five years we think is an encouraging indication of where we're going.

Andrew Schorr:
The standard now, at least when somebody comes to your institution, is you want to understand that patient's specific situation, not just where the cancer is but really understand the biology and then begin a plan that's right for that. So tell us how that works. We talked about this VATS or video-assisted thoracic surgery to get I believe a sample of the tumor in [Ruth's] lung. I imagine that went to a pathologist, so that's all part of this, right?

Dr. Johnson:
That's right. Here at Northwestern and at many other academic institutions

nationwide, worldwide, we agree that most important part of a patient's initial workup is the molecular analysis of the tumor to see if we can identify up front any oncogene drivers that are causing the lung cancer development. Ruth's case is an excellent example of this.

She presented with metastatic disease that had gone to her bone, and we did a biopsy of the bone that proved that she had a lung cancer that had gone to her bone, and so 30 years ago that would have been more than enough tissue and information to start treatment, but I actually asked Ruth to undergo not just one but two additional biopsies in order to get enough tissue to test for EGFR, to test for ALK, in order to select the best treatment plan for her.

Both at the beginning of treatment and subsequently now as we develop more and more targeted agents, patients are being asked to undergo biopsies during their therapy so that we, the lung cancer investigators, can begin to understand the genetic changes that occur after treatment that will help inform future therapies that are currently in development. So, unfortunately in Ruth's case the oncogene that's driving her cancer, it's been a little bit elusive, and so while I know in my heart and in my gut that she has a mutation driving her cancer we have not yet identified it because it's not one of the ones that we are testing for currently.

Andrew Schorr:
But you were saying related to ALK that that was only identified just a few years ago.

Dr. Johnson:
That's correct, and there are several other mutations or oncogene drivers that are being investigated, among them KRAS, which actually we've known about the presence of KRAS mutations in lung cancer for 30 years, but we have not yet been able to development a successful way to target or turn off a KRAS mutation. Also BRAF mutations are an important subset that we are investigating. HER-2 mutations are an important subset that we have identified. PIC(3)CA mutations are an important subset that we are identifying, and the identification of those mutations are still being done experimentally. They are not approved for widespread use, and likewise the drugs that target those mutations are still being investigated in clinical trials.

Andrew Schorr:
I just want to mention something about clinical trials, and you're at an academic center. So I was treated for a leukemia and did go to an academic institution and did participate in a phase 2 trial and got a new combination therapy and it was successful, fortunately, that's why I'm here, and I received that 10 years before that combination was approved by the FDA. So I would urge people, and I think you'd agree, Dr. Johnson, that clinical trials, in lung cancer that's something that should be put on the table and the patient and the doctor discuss it at least to see whether that's a right option, right?

Dr. Johnson:

Absolutely. Absolutely. Thank you for that plug, and I would echo it that we are at the--we are at a point in our understanding of lung cancer where clinical trials are often an amazing opportunity to help not only push the field forward, push forward what we know but also gain access to experimental drugs that really have a rational mechanism by which they may help stop lung cancer growth.

Andrew Schorr:
Let me try something out on you. So when we talk about tailored or personalized therapy and you identify the oncogenes in this case that are going on with a patient and you give them what we like to see as targeted therapy, that also means that they're being spared some of the more shotgun approaches that you had earlier before you had that knowledge, and with them came certain side effects. So in a sense the patient may be spared that because you have a more precise knowledge of their situation. Is that right?

Dr. Johnson:
Absolutely. I'm glad you brought that up because that is another benefit of targeted therapies. In the past chemotherapy, traditional chemotherapy agents, worked by inhibiting the growth and division of rapidly dividing cells, so all the cancer cells in a patient's body are rapidly dividing, but so are hair follicles and so are gastrointestinal, stomach and intestinal lining. So with hopefully antitumor effects there was a concurrent side effect profile that hit all of the rapidly dividing cells in the body. But these targeted therapies are just that. We hope this they work exactly on and nowhere else in the body other than the cancer cells.

Andrew Schorr:
And let's just talk for a minute about one of the drugs that Ruth's getting, Avastin. So the idea there is to cut off the blood supply, the unique blood supply that cancer cells develop, and if you can cut off the blood supply you can limit the growth of those cells, right? So that's an example of a targeted approach, too, right?

Dr. Johnson:
It is. It is an example of a targeted approach. And it has been developed in a number of different tumor types, some with more success than others. Often patients will come to me and say, now, wait a minute, I've read about this drug, and it gets less than favorable ratings in breast cancer patients, for example. And so again I would say that this is an example of personalized therapy. Every patient and physician together work collaboratively to come up with a treatment plan at Northwestern, and it's very important the type of cancer that you have and the biologic properties of that cancer in developing a treatment plan.

Collaborating with Your Medical Team

Andrew Schorr:
Right. And I think as we saw with Ruth--I know you were overjoyed to hear that this combination therapy you have been receiving has shrunk the tumors so much, so that's great. But somebody else might receive the same combination, and their body didn't respond quite so well. So people vary even when there might be on the

surface things that look the same, right, Dr. Johnson?

Dr. Johnson:
Yes, that's true too. I tell all of my patients at the very beginning, "I don't know how this therapy is going to work for you until we give it." And so I encourage my patients to really play an active role in their treatments. I think having a collaborative relationship between patient and physician is an incredibly important part of personalizing therapy. Patients need to be able to report the side effects that they're experiencing. They should understand, not only the chemotherapy medicines that they're receiving, or the anticancer treatments that they're receiving, but their other medicines. Because that will aid the communication between the physician and patient and help future modulations of treatment, for example, increasing or decreasing the doses, increasing or decreasing the number of medications and deciding also when a treatment plan is no longer working and when a new one should be selected.

Andrew Schorr:
Let me ask you about this term "multidisciplinary care." So, Ruth, let me see if I got this right. So you started out with a sports medicine doctor, Dr. Edwards, right?

Ruth:
Yes.

Andrew Schorr:
Then you had another orthopedic surgeon come into play with the tumor on the femur. That was Dr. Peabody, right?

Ruth:
Right.

Andrew Schorr:
Then you had radiation.

Ruth:
Right, with Dr. Marymont.

Andrew Schorr:
You had Gamma Knife, you had different kinds of radiation, and you also had the video-assisted thoracic surgery to get the biopsies of the tumors, so that was a lung cancer surgeon, right?

Ruth:
Mm-hmm.

Andrew Schorr:
And you had your medical oncologist, your thoracic specialist, Dr. Johnson, and behind the scenes I'm sure there were pathologists and radiologists, and it's quite a

big team that comes into play, isn't it?

Ruth:
It is. The thing that impressed me is that they actually talk to one another, because I mean as a patient, especially someone if you're not familiar with how it all works in the background, to know when you go to an appointment your doctor says, "Okay, I talked to Dr. Johnson and she said this and we discussed it and this is what we decided." I mean, they actually work together to find out what's best for you.

Andrew Schorr:
Dr. Johnson, can you tell us what goes on in your meetings of all these people?

Dr. Johnson:
Sure. Well, it's a very important part of our philosophy of cancer care here at Northwestern that each patient should be presented in our multidisciplinary conferences. We meet once a week and we discuss all of the patients that we share. And you're right; it doesn't just include the clinicians, the orthopedist, the radiation oncologist, the medical oncologist and the thoracic surgeon. Very important members of our team are the radiologist who specializes in reading the chest CTs, for example, pulmonary films, as well as the pathologist who specializes in looking at tissue that has come from the lung.

And this is another reason that I would urge listeners to think about at least a consultation if not pursuing care at a place like Northwestern. At an academic center you gain the expertise of all the people that are working together towards devising a treatment plan. So you benefit from the subspecialty training that physicians at academic centers have received as well as an experience in a specific area which, as compared to physicians who see all sorts of diseases or all sorts of cancers, it is a unique opportunity.

Andrew Schorr:
Right. And also this is often where there's the greatest selection of clinical trials where a lot of the research starts.

Dr. Johnson:
That's absolutely true. And we can plug the clinical trials program again here at Northwestern. I wanted to also mention that a number of our clinical trials here are genotype-specific trials, so they are tailored toward patients that have a particular genotype causing their tumor, and in this way we really are excited about, the therapeutic strategies we may be able to bring to the forefront or--and have approved for more generalized use.

Ruth's Advice to Other Patients

Andrew Schorr:
Ruth, I want to ask you a question. I kind of telegraphed it at the beginning. So you have to get your head around this as a patient, and you kind of rattled off, you

know, the treatments you've had and the doctors who came into play, but in the background is, you know, facing a very, very serious illness. How have you dealt with this? And do you have any guidance? I mean, everybody is different, and they're going to respond differently, but things that have worked for you as you're going on with your life?

Ruth:
Sure. Well, I think whether we want to talk about it or not, if you're faced with a stage IV lung cancer diagnosis, I mean, one of your biggest fears is death. I mean, none of us are really comfortable with it, I don't think. And so as a budding sociologist I took a look at the literature, and I examined it sociologically. I looked at psychology, medicine, spirituality. I also looked at some illness narratives, so reading stories of people who either they or people they cared about were suffering from life-threatening cancer or things like ALS to basically come to terms with death. And for me to become comfortable with death allowed me to kind of let it go so that I could live, if that makes sense.

Andrew Schorr:
Yeah, it makes perfect sense.

Ruth:
I'm not going to say that's going to work for everyone by any means, but it certainly worked for me.

Some advice that I might have for other people, physically I think good balanced diet and exercise. I know that's drilled in our heads since we're little, but it helps keep up your resources so that when you're going through treatments it helps you get through them, helps your body stay as strong as it possibly can. I think that was--is probably one of the major things that I've done physically.

Mentally, I think, thinking of cancer as a chronic disease like heart disease or diabetes is helpful. It's just something that you live with. You have to go to your treatments and perhaps you have to modify your behavior a little bit, but you still live your life.

Andrew Schorr:
And how do you view the future?

Ruth:
That I think is probably one of the toughest things you have with stage IV, and that came out in the literature too is that at one point you could see this future--I mean death was this distant thing, but a lot of people talk about having no future or [that] it's difficult to negotiate life because of this blank like this. It's a very different way to live, so what you do as a consequence is, as much as you can, live each day as it comes.

Andrew Schorr:
Right, but when you were told that you had, you know, cancer that spread in all

these parts of your body you didn't know that you'd see the day when these drug therapies would come together to vastly shrink the tumors, right? So the future can have some promise, too. You just don't know.

Ruth:
It can indeed, and in fact my husband and I often have discussions about, you know, we're just waiting for the next therapy to come through that will be able to have some effect.

Andrew Schorr:
Well, I hope so. And Ruth Ashton, we want to wish you all the best, and we thank you for participating.

The Future of Personalized Therapy

Andrew Schorr:
I want to give the last word to Dr. Johnson, because, as you said, you're waiting for the next therapy.

Dr. Johnson, a specialist such as you and at a research institution, you're kind of a barometer, you know. How do you feel about the way things are going in our fight against now specific subtypes of lung cancer?

Dr. Johnson:
You know, it's funny because you say that I'm the barometer because that--it's people like Ruth that are my barometer that we are making progress. She had her one year cancer-versary just recently, and look, she's got metastatic lung cancer yet she's working and living, and that's what gets me out of bed every day.

Looking forward, I am very excited about the number of oncogene drivers that we are identifying. I think targeted therapies that will turn off the lung cancers that are started by these mutations are just around the corner. So what I see as the future and actually it's already the present at some leading institutions in the country, but there is a panel of mutations that are part of any patient's workup. Looking forward, maybe we won't even have to sample the tumor. Maybe we'll be able to do it just with a blood test, and based on those results tailor a treatment plan like a Chinese menu. So one angiogenic therapy, one anti-EGFR therapy and one anti-insert the mutation here therapy together, a combination of treatments up front I think is the future.

Andrew Schorr:
Wow. Just all the best for you, your colleagues in science and in the clinic in helping bring that to bear for our new friend Ruth and others who are listening who are affected by this. Dr. Melissa Johnson, thoracic oncologist at Northwestern Memorial Hospital in Chicago, and Ruth, all the best. My dream is you're going to be able to play with those grandchildren for a long time, okay?

Ruth:

Thank you. I hope so, too.

Andrew Schorr:
Thank you so much for being with us. This is what we do on Patient Power is come head-on and discuss serious health conditions and really survey where we are and meet inspiring people like Ruth and inspiring physicians like Dr. Johnson who are right in the trenches working to make our care better.

I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.