The Proactive Lung Cancer Patient: How to Get Tomorrow's Medicine Today

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Andrew Schorr:
Hello, and welcome to this worldwide, certainly nationwide broadcast. I'm Andrew Schorr with Patient Power in Philadelphia. And this program, of course, is "The Proactive Lung Cancer Patient: How to Receive Tomorrow's Medicine Today." And we're joined by an expert panel of physicians, and also, aptly, longer-term survivors with lung cancer. And this will be a very informative and inspiring 90 minutes. Remember, you can send your questions in at any time to questions@patientpower.info. We'll be posing those to our experts. Of course, the whole field of lung cancer has been changing. And so, as this science is improving, happily, it's so important now for you and the family to really take a greater role in your care. And we're gonna talk about that throughout our whole program.

I want to thank the wonderful organization that's really enabled us to put this on, and that's SURVIVEiT in surviveit.org. And they've just been great. And you're gonna meet, in a minute, the founder of SURVIVEiT, a survivor in lung cancer, Matt Ellefson. We also want to thank our sponsors who provided funding for this program, Celgene, AbbVie, Foundation Medicine, Novartis, Guardant Health, and then with additional support for Viviphi. So thank you so much for helping make this program possible.

Okay, what are we gonna do during this program? You've been learning that you can send in questions. We have downloadable resources for you that were on the registration page, but we'll email them to you as a participant afterwards. And that will help you with a glossary of terms, and let's face it—I'm a two-time blood cancer survivor. When you're diagnosed with cancer, there are all these acronyms and terms and medicines that you've never heard of, and you're terrified. And so, we have a glossary prepared for you.

There's also a guide that SURVIVEiT has helped provide for you, a Start Here guide. There are questions to ask your doctor so that you get state-of-the-art care that's right for you. There's also a guide to how to get remote second opinion, which can be often very important in lung cancer now. And then also, a patient guide that was prepared by one of our supporters,

Foundation Medicine, and we thank them for that. Okay. Let's meet who we have with us today. And really, we're so delighted that they could take the time to be with us. First, I want to go to—I believe it's Fairfax, Virginia, and introduce Dr. Alex Spira. Dr. Spira is with Virginia Cancer Specialists. He's the Director of the Virginia Cancer Specialists Research Institute in the Phase I trial program at Virginia Cancer Specialists. Dr. Spira, thank you so much for being with us.

Dr. Spira:
Thanks, Andrew. Glad to be here.

Andrew Schorr:
Okay. Now let's go up to Boston. We have another eminent physician and specialist in lung cancer, and that is Dr. Bruce Johnson. Dr. Johnson is the Chief Clinical Research Officer and Institute Physician. He's a Professor of Medicine at Harvard Medical School. He is at the Dana-Farber Cancer Institute, and also, he's just been installed as the President of the American Society of Clinical Oncology. Dr. Johnson, thank you so much for being with us.

Dr. Johnson:
It's great to be here this afternoon, Andrew.

Andrew Schorr:
Well, of course, this program is for patients. And so, we want to include some inspiring patients with you. And so, first, I want to introduce you to, from SURVIVEiT and from Sioux Falls, South Dakota, Matt Ellefson. Matt has had quite a journey with lung cancer, and is a great inspiration to people all around the country, all around the world. Matt, thank you for joining us. And how long have you been living with lung cancer now?

Matt Ellefson:
First of all, I'm very glad to be here, Andrew. And I've been living with lung cancer, stage IV lung cancer, that is, for seven-and-a-half years.

Andrew Schorr:
Whoa. And it started with a cough, right?

Matt Ellefson:
It started with a cough, and then it turned into coughing up blood. And my prognosis was very grim. I was given eight months to live. And now, here I am, almost—I'm working on my eighth year of survival, and I'm just very grateful for that. And I'm really grateful to pass on how I was able to do that, and this great panel of experts that are here today that are gonna talk to us about their viewpoint on how to survive cancer.

Andrew Schorr:
Right. And we're gonna learn more about—you've been in clinical trials, and we'll talk about that along the way. You've had genomic testing. We'll talk about that along the way. Okay, so I've gotten to cover sort of as a medical reporter, some of the lung cancer meetings, the World Lung meeting. There are others that happen throughout the year and around the world.

So I think let's start with an update for patients affected by lung cancer and their family members to kind of get the latest on what the news is and research in learnings about lung cancer and diagnostics, and what it means for patients. Dr. Spira, I want to start with you. And from Virginia Cancer Specialists, sir, tell us about what you see, how you see the landscape changing, and what it means to people knowing that there are different types of lung cancer. But maybe first overall, and then if you want to call out specific progress that you think is particularly meaningful.

Dr. Spira:
Sure. So, I think one of the things that we really learned in the last 12 to 36 months, and ASCO this year is no exception, is that lung cancer continues to be multiple different subtypes. So we've gone many years from just non-small cell to squamous and adeno. But the tumor subtypes, looking at genetic mutations the drive a lot of tumors, EGFR was the first one. We have out mutated lung cancer. We have BRAF now.

We have RET mutated. We have MET amplified, MET mutated. So, I think the biggest take-home message is the importance of looking at the genetic analysis of tumors, getting enough tissue to analyze tumors, and really trying to define the right drug for the right patients. At this point, not every patient is going to have a specific subtype. We're learning more and more as time goes forward.

Andrew Schorr:
All right. Well, thank god there's progress in lung cancer. So, Dr. Bruce Johnson, you've been a research in the field. Like Dr. Spira, you've been devoted to it your whole life, and you helped lead the research program there. And of course, you have a mission now as president of ASCO so that as we learn about these different subtypes—and Dr. Spira just said it—so patients can get what's right for their version of lung cancer. Tell us about the mission of so-called precision medicine. Where we are with it today, how precise is precision medicine in lung cancer, and how does someone get it wherever they get there?

Dr. Johnson:
I want to start giving a little bit about how this has evolved. Both Dr. Spira and I have been at this for a while. And this began to change about a little bit longer than a decade ago, when I was proud to be a member of one of the teams that discovered the genetic changes or the mutations in one of the genes called the epidermal growth factor receptor. Its normal function is to control the growth of skin and other areas that line your lungs and gastrointestinal tract. And we learned, starting in 2004, that you could give a pill instead of chemotherapy, and it's present in about 10 or 15 percent of people that have adenocarcinoma. It's among the most common type of lung cancer that Dr. Spira talked about. And then, as he mentioned, it's going on from there, where we've added additional genes.

The ones I think that are pretty critical to test for now are ones where there are approved drugs. And so, the ones that I think are particularly critical that almost all of our patients who have lung cancer should do is to be tested for four that have genetic changes where there's approved drugs, and that's mutations in the epidermal growth factor receptor, EGFR. The second most common is one called a rearrangement of a gene called anaplastic lymphoma kinase. Now, we're talking about lung cancer here, so the anaplastic lymphoma kinase was discovered in a lymphoma initially in childhood cancers. But it turns out it's also rearranged in lung cancers in about 5 percent. And there is a number of agents for that. And in a little bit, we'll talk about what we learned at this year's meeting.

And then the third one, that has already been mentioned, is one called ROS1. And that makes up about 1 percent. So, it's sort of coming in smaller increments, going from 10 to 15, five percent, one percent. But when you add those up, you're getting close to 20 percent. Then, as Dr. Spira mentioned, the latest one that's likely to be approved soon is one that we've known as effective treatment in melanomas, and that's a gene called BRAF that's mutated in another one percent. And we anticipate that it's likely gonna have approval. So those are four different genes. Now, we'll come back in a minute about the impact of immunotherapy, both from a patient perspective as well as those of us that work in the field.

Andrew Schorr:
Dr. Spira, so you have research going on that you help lead at the community level throughout the country. So, the question is, who should be tested when? It sounds like there could be a zillion genes. I don't want to say a zillion, but I know there are many more genes that you don't know are actionable now. So what are you saying your program now as far as who to test and when?

Dr. Spira:
We recommend testing of everybody, certainly with adenocarcinoma. Those tend to have a much higher predilection to be driven by one of these mutations. We call them driver mutations. I actually test almost all my patients, because you never know what you're going to find. As you heard from Dr. Johnson, there are about four basic ones that we can see. There's a smattering of other ones, which are either on guidelines, commonly known about, or you can actually find clinical trials. And these are—for example, there's one on CMet called a skipping mutation. And even though it's relatively rare, it has been seen, and there's a lot of clinical activity. So I pretty much test all my patients right now with lung cancer when we can get enough tissue. Everybody does things a little differently.

Certainly, the basic ones that you see make up the majority, those should be tested in everybody. But I think a lot of us are now migrating to testing those things that we have out there that's about five to 10 genes currently.

Andrew Schorr:
Now, Dr. Johnson, so what do you say about testing? And I know that still—I know there have been surveys that still, throughout the country, a lot of people aren't being tested. And I know there are issues about whether insurance will pay for it. There's a lot of stuff. But what are you hoping can be accomplished in the cancer treatment world to help people know what they're dealing with and whether it's actionable?
Dr. Johnson:
We think it's pretty critical. And one of the things that we've done at both our centers and all the major centers is for a decade, we've been testing for multiple for at least 10 different genes. And it's now expanded in 2013 to somewhere between two and 400. Now, once of those is a for a very practical reason, and that is that each additional test that you do, if you're doing it sequentially, you have to retrieve the tumor tissue. Have to send it off for testing. And what you want to do is try to be as comprehensive as possible with the initial test. And one of the things that's offered, there's a large number of commercial providers, including one of the sponsors to this, that will do these very large hundreds of gene panels.

And one of the things that is difficult to predict is which of these is gonna be an effective target? As Dr. Spira mentioned, one of the ones, and one of my colleagues, Dr. Awad, has published a number of articles on, what Dr. Spira described as exon 14 skip mutations of MET. And there are effective drugs for it. And I just had a patient over the past week who was tested several years ago when we didn't know the association was a predictive marker of the benefit of the drug. And it was buried in the other material that we didn't know, and we were able to identify it for the patient and consider that targeted therapy. So we think that you should have a brought panel. You should test everybody with adenocarcinoma. B) you never know which of these is gonna be informative, not only now, but into the future.

Andrew Schorr:
Right. I want to just go to Matt for a second, and then I'm gonna introduce you to another patient who's very inspiring. Matt, so you're a big believer that people, knowing that sometimes lung cancer, biopsies, tissue, that's precious stuff that you want, you would urge patients to see if they can be tested and be tested for a broader panel, just like Dr. Johnson was describing, correct?

Matt Ellefson:
Exactly, Andrew. And the reason that I believe that so strongly is you never know when you're gonna be able to get that opportunity again to test. And I've been in that position where the metastases or where the recurrence has occurred is a very invasive surgery, to be able to grab a tissue sample. And I wasn't well enough as a patient at that time to really undergo a major surgery like that to get the biopsy.

And so, if I hadn't have known—hadn't have had a complete panel, it would have limited my medical team that I was seeing, my team of oncologists who would have limited their knowledge and their abilities and the tools that they had available to be able to help me. And then the other thing that comes into play is—and I would hope that both Dr. Spira and Dr. Johnson would explain this in more detail—but another thing that we're hearing more and more about are drug cocktails, where I, for example, have the ALK rearrangement, but I also have another gene that they feel may be contributing to my cancer in some way that has an approved therapy for breast and ovarian cancer, but not for lung cancer. And so, if I did an off label drug cocktail of the two drugs, then that may be beneficial to me.

But this is all relatively new, so I'm really excited to hear what Dr. Johnson and Dr. Spira have to say about this, because I think it's really important. I think it's not only important to get that comprehensive diagnostic testing immediately when you're diagnosed or to set your baseline, but also as you have recurrences, if you have the ability to go in and get another biopsy without harming the patient or making his or her condition worse, I think that's also very important, because things change over time.

Andrew Schorr:
Right. I wanted to bring that up with Dr. Spira. So, Dr. Spira, we have people who may be newly diagnosed who are with us. And so, you're talking about testing. But hopefully, people live longer on their journey with lung cancer. So can these genes mutate, change, and so there's a reason to do a testing again at some later time?

Dr. Spira:
Absolutely. We already have a great example for that. As Dr. Johnson talked about, the EGFR gene, people start with one typical mutation, and patients develop the secondary mutation in that. And we thankfully have an FDA-approved drug called osimertinib (Tagrisso) that can target that as well. So, absolutely. You also learn a lot. You also might learn when a drug is not working, and how far to push things as well. So, it's also important to know when to switch to a different drug also. So, absolutely, we are getting routinely follow-up biopsies in our patients right now. And it's challenging, because a biopsy, as Matt said, is an invasive procedure. But it often can provide very helpful information to us.

Andrew Schorr:
Okay. One other question about studying the genes that may be at work. So, in the last year or so, we've had the development of liquid biopsies, testing from the blood.

So, where does liquid biopsy, Dr. Spira, fit in now with testing the actual tissue?

Dr. Spira:
So liquid biopsies have really revolutionized a lot of what we do. They're not perfect in all patients, because obviously, in the blood, you're only measuring what you can measure in the blood. You're not measuring the tumor, per se. For those of you who don't know what a liquid biopsy is, it's essentially a blood test where we're taking a sample of the blood and relying on a tumor to shed either DNA or RNA that you can measure in the blood. So it's been a great help for patients. I've had many patients where we couldn't get a biopsy, or the biopsy didn't show something, but you can actually measure it in the blood. And a blood test is certainly a lot easier. The only challenge is that if you're not knowing something, you don't know if you're not showing something, because you don't have it, or because you just don't have enough tumor specimen to measure in the blood. But it's been a great thing, and we do it in our patients routinely now.

Andrew Schorr:
Okay. So, Dr. Johnson, I don't want to forget. We've mentioned adenocarcinoma. We talked about non-small cell lung cancer. There's a minority of lung cancer patients who have what you call small cell lung cancer. And we were talking about sort of cancer news. Is there some news in progress for them?

Dr. Johnson:
Small cell lung cancer was the first type of lung cancer I worked on when I began my training in 1982. And one of the things there was great promise, the first article I ever published was on people who survive five years or longer after getting treated for small cell. And actually, some patients are cured with conventional combination chemotherapy. That was known back in the 1980s, and there was great hope. One of the things that's been relatively complicated is that after they did a rather systematic genomic characterization of small cell lung cancer that was published about two years ago. There are not very many genes that are effectively targeted that you can identify by doing the comprehensive panels and doing comprehensive sequencing of those specimens.

There has been—there are two important potential advances that agents that are still in trial. One is called Rova-T. It's a recombinant molecule that's directed against—and when I say recombinant molecule, what they do is they take an antibody. That's a molecule that recognizes a specific epitope, or a determinant on the surface of the small cell lung cancer cells, and they covalently link it to a poison or a toxin. So it becomes kind of a magic bullet that's targeted there. And about 40 percent of the patients who get this who have lots of the stuff on the surface of the cell that this agent is directed against will have their tumors shrink. And it's now being tested in a large trial.

The second one that's being tested a bit more widely is another molecule that's similar to that. And the stuff that's on the surface of the small cell lung cancer cell happens to be called somatostatin. And this particular agent also binds preferentially to the small cell lung cancers, and can help target it and get this poison. And we're waiting to see. That one's in a bit earlier trials. But certainly, the experimental evidence that this could work is pretty compelling.

Andrew Schorr:
Mm-hmm. So, Dr. Spira, so you helped run a research program. So the title of our program is talking about tomorrow's medicine today. So people have been in trials, and I've met them, where they were, quite frankly, near death, and they had a remarkable resurgence, if you will. And Matt's been in trials.

So, as Dr. Johnson is talking about what's in research or even early research, like you do Phase I trials, what would you say to people about considering being in a trial with the pace of research that's going on?

Dr. Spira:
So the only way we get better treatment is by doing clinical studies. I mean, that's kind of the bottom line. Occasionally, you hit home runs. And a lot of these targeted therapies, many of my patients, and I'm sure Dr. Johnson's patients, got when they were on a clinical study. You may have had a hint of activity. You may have had no hint of activity, and it just made sense. They are great options for patients that want to participate. They're great options for patients who run out of options. I mean, despite our great advances over the last decade, many of our patients still run out of options and are looking for something better. And that's what they were all about. It's either gonna be new drugs, new combination immunotherapies, new combinations of targeted therapies.

But for those patients who are interested, it's a wonderful opportunity to help fight their cancer, and of course contribute to science as well.

Andrew Schorr:
Okay. Now, Matt, you've been in clinical trials. I have too for blood cancers, but you've been in for lung cancer. What would you say to people about that? I mean, a lot of people say, look, is it a gamble? Maybe there's been a standard therapy that maybe has worked for people, and I want to stick with it, or what would you say? And what was your decision-making about being in a trial? Because a lot of people and family members are afraid of it.

Matt Ellefson:
You're absolutely right, Andrew. A lot of people are afraid of it. And what I would tell them is not to be afraid of it, because in today's day and age, it's a lot different than it was 20, 30, 40 years ago in a clinical trial, these trials are run very, very safely.

They are oftentimes run in a drug or in an environment where they have an enormous understanding of how this medicine or this drug had performed previously in the lab, and they've had some really compelling results with that. And so, it isn't as big of a risk, I believe, than it was many, many years ago. It's more like now they're zeroing in on things, whereas before, some of those clinical trials were more like a shotgun approach. Today, they're more like a rifle approach. And I wouldn't hesitate one bit to enter in another clinical trial. They've been quite—I've done really well with them. And as a matter of fact, I believe that they've saved my life twice, and I'm very grateful for the work and the innovation and the research that's going on by all these doctors and large cancer centers.

And I'm just grateful to live in a place in America where we have access to clinical trials, because so many people don't. And we really need to take advantage of those.

Andrew Schorr:
So, Dr. Johnson, you're at a big NCI comprehensive cancer center. Dr. Spira, you're one of the leaders throughout a whole community oncology network throughout the country. Increasingly, there are trials offered not just at your clinics in Virginia, but with some of your peer clinics around the country, right? And that's something that people can inquire about, correct?

Dr. Spira:
Absolutely. And there's a lot of oncology research, not just at the big NCI-designated centers, as you said, but at a lot of community-based places as well, which is nice for patients so they don't have to travel if they want to do this.

Andrew Schorr:
Okay. All right. Well, let's go on. And you mentioned it along the way, Dr. Spira, and I want to ask Dr. Johnson about it. And that is, you were talking about immunotherapy or immuno-oncology.

Let's face it, there are TV ads on now that probably many people in the lung cancer community have seen and said, does that apply to me? So, Dr. Johnson, first, a little bit of a science lesson. What do we mean when we say immunotherapy, and how do we know who it applies to?

Dr. Johnson:
So, immunotherapy—and what we're talking about has been tried for decades in cancer. And one of the things that was pretty disappointing up until about two or three years ago is the times at which it worked in cancer, and in particular lung cancer, were pretty meager. And one of the things that we began seeing two or three years ago was patients who were beginning to respond to the therapies. And one of the things I say to my patients is that it's one of the few times it's relatively good to have smoked, in that people who have smoked cigarettes are actually more likely to respond to it than people who haven't.

And the reason we think that's the case is because the immunotherapy is working against mutated products in your cancer that aren't present in your normal tissues. And one of the ways that cigarette smoking causes cancer is it causes your normal genes to mutate. And that's what makes it become a cancer. And because 85 percent of the people who get lung cancer are people who have either smoked cigarettes in the past or are current smokers. Now, one of the things we began seeing is, in people who'd been heavily pretreated, we began seeing a few responses. And then the randomized—the studies that studied giving chemotherapy versus immunotherapy were published about two years ago, and became more widely available in the last one to two years. And it gave another option.

And there are two things that are pretty incredible about the immunotherapy. And that is that there's a subset of people who not only respond to it, but it looks like it's going on for years. Julie Breamer has been one of our leaders from Johns Hopkins. And she updated the data at our national meeting, and showing there's in between ten and 20 percent of the people are alive at three to five years, which is pretty unusual for advanced lung cancer, which both Matt—which Matt Ellefson has pointed out to us. The part that has, to me, is the biggest change in lung cancer is the initial treatment. And one of these types of immunotherapies, and as you mentioned, it's also advertised on television, is called Keytruda, or pembrolizumab.

And in that one, if you study the tumor and find out that more than of the cell have a marker associated with high levels of response to pembrolizumab, you can get that as an initial therapy instead of chemotherapy. And in those patients, say, a little longer than if you got chemotherapy. And that's one of the things we now test our patients for. And as Dr. Spira said, we break this down into different subsets. Those that are greater than 50 percent, and the marker's called PDL1. Those that are greater than 50 percent PDL1 positive should get immunotherapy rather than chemotherapy because they live longer. We're also hopeful that these are also the patients that are gonna—we're gonna see a subset of them have long-term survival when we follow them longer. When we talk about—we only have about three or four years of follow-up with these patients, so we're waiting to see what happens as this matures.

Andrew Schorr:
Let's meet somebody. So I wanted to introduce another patient. And your comments now about immunotherapy are very appropriate. Joining us from Northern California is Don Stranathan, who has just had his 35th infusion of one of these immunotherapies. In your case, it was nivolumab (Opdivo), right? Don, thank you so much for joining us. How long have you been living with lung cancer now?

Don Stranathan:
Since 2009, June of 2009, the 23rd. So, next week'll be eight years.

Andrew Schorr:
Wow, wow. And good for you, Don. And then you've been having this immunotherapy. How has it been for you as far as side effects or just managing it going on with your life?

Don Stranathan:
I've been very fortunate. I was on a targeted TKI erlotinib (Tarceva) for six years, and then I went on and got genomic sequencing when I had progression in 2015.

So I found out I had no driver mutations, no EGFR, no ALK, and got a second opinion, and it was suggested that because I was a former smoker, I had moderate expression of the PDL1, just over 1 percent. But those factors, they thought I'd do very well. And just had my 35th infusion yesterday, and still have stable disease. The only side effect is I've had some thyroid issues, and I'm on a thyroid medication. But that's under control.

Andrew Schorr:
Right. I should just mention one thing. Two things with Don. One of them is, if you have a question, it's gonna go to Don. Send it to questions@patientpower.info. And I don't mean to trivialize it. Don's sort of gonna be our Vanna White. We're gonna go back to him, and he's gonna give us questions from the audience—so questions@patientpower.info.

One thing about Don is, Don, you fell in love with someone you met through an online group for lung cancer, Penny. And that made a big change in your life. I know she passed on a couple years ago. But that was not only your long life, but it led to love as well, and I think that's a remarkable story.

Don Stranathan:
Yeah. And I'd like to thank Dr. Johnson. I was just featured this issue in the ASCO Post. They ran my story on how Penny and I met on social media, so, yeah. That's been my passion, to advocate for lung cancer. That was my last promise to her, that I'd continue to advocate for more research and awareness of lung cancer.

Andrew Schorr:
Right, right. And as we saw with Penny, unfortunately, too many people pass on. So, we've gone through some of the science. We're gonna come back and do more. But, and Don, we'll hear more from you along the way as people send questions at patientpower.info. And we have some that have come in.

Matt, so, we talked about testing. We talked about trials. You have a lot of wisdom, as you've lived with this over the years. And we'll ask Don too. What are some pointers that you would say to people as this science is changing? Is it immunotherapy? Is it these mutations? ALK? EGFR? BRAF may show up, and there are other ones that Dr. Spira said they're identifying, and all the ones that Dr. Johnson said they're testing for so many more for the future. So, wherever you are, if you're in Sioux Falls,— South Dakota. If you're in Carlsbad, California, where I live. If you're in Philadelphia, where I am now, what should people—what kind of discussions should they be having with their doctor?

Matt Ellefson:
I think, Andrew, that's a great question. And I think first and foremost, people need to ask to have their tissue tested for genomic sequencing, genomic profiling, whatever you want to call it—it's the same thing—to find out just what is driving their cancer, if possible.

Because it's really hard. It doesn't matter what we're doing. We can't fight an enemy until we know what the enemy is. And once we understand what it is that's driving the cancer—and sometimes, I realize sometimes you aren't gonna be able to find that out. But I think in most cases, they do identify something. And that provides that patient with the opportunity to get on a drug therapy that is tailored just for them. And it's what precision medicine is all about, as opposed to when I was initially diagnosed, they were still treating patients with different chemotherapy infusions, and it's not that those aren't effective. Those can be. But that again is kind of a broad-based approach based on the amount of patients that respond to that type of chemotherapy for that particular type of cancer.

Whereas now, when we go into precision medicine and we're talking about genomic profiling, genomic sequencing, we can target just exactly what it is. And then oftentimes, if some other gene abnormalities show up, the doctors and the researchers will know really what pathway is contributing the most to this cancer, and what genes are on this pathway that can also affect it in some way. And that is—to me, that is critical, because if you get on the wrong therapy right away – well, it doesn't matter when it is. If you're on the wrong therapy—therapies take a hard toll on your body. They really do. And over time, a patient or a human being can only—we can only tolerate so much. And our body—our organs and everything just kind of get worn out.

So it's really important that you do that immediately right away. And if you are a patient that hasn't had genomic sequencing, and you've been diagnosed with cancer for a couple of years now, it's not too late for you to ask to have that

sequencing done. And I would urge everybody to do that. The second thing I would urge people to do is get a second opinion in an academic research center. And the reason why I say that is there are so many community cancer centers around America that have great doctors. They're doing great work, but they just don't have the tools that some of these big academic research centers have. And they don't see the caseload. They don't see the amount of patients that some of these larger academic research centers have. And so, you need that experience from your medical team, especially if you have kind of a tough situation.

If you're a patient that has a gene abnormality that only occurs in 5 percent of lung cancers, then it's not going to be seen very often by these community cancer centers. And some of the bigger cancer centers see more of that, and they know how to deal with it better. So, it's worth—to me, I think that it's worth every penny you spend on getting a second opinion and really having another team look at your case really thoroughly, a team of experts. And then hopefully, they can put together a protocol for you. They can collaborate with your doctor at home, at your community cancer center. And you can go home and have that treatment administered and delivered to you in your hometown.

Andrew Schorr:
Right. Now, I want to mention, Dr. Spira is really one of the leaders in lung cancer within a big network called US Oncology Network, and certainly the Virginia Cancer Specialists throughout suburban Washington.

So, Dr. Spira, I wanted to ask you about two things. First of all, for the community oncologists, you're running a research program, but somebody—and I used to go to an HMO in Seattle—that doctor had to take all comers. And now we're talking about the pace of change in lung cancer, melanoma, in leukemia and breast cancer. It's hard to keep up. So, I'm sure they look to you often as a guide as well. What would you say to patients about second opinions? And I know even on our website, we're helping people understand what institutions even give remote second opinions. Maybe Dana Farber does that, Dr. Johnson. So, Dr. Spira, what would you say about first of all being a partner with your doctor to uncover what's right for you in a changing landscape? What comment would you make?

Dr. Spira:
So, I think, I mean, second opinions are always—everybody should welcome them, and everyone should get one if that's what they want.

You're right, it is challenging. I mean, the field has changed dramatically. There are a lot of rare mutations. And certainly either going to a place that sees a lot, be it a lung cancer expert in the community, be it at an academic medical center, whatever one finds, I think, is exceedingly important. Because as you heard, you're right. There are super rare mutations, and there are things that you never heard of before. And there are lots of rare things you should be thinking of and just asking the question. I think remote second opinions where offered are great then, as long as everybody feels comfortable with that. There is still a role with interacting with patients. I mean, we all get emails all the time from somebody, "My mother has X. What do you think?" And it turns out, the patient's not really a candidate for the therapy. But certainly, for the newly diagnosed, that is a changing world and landscape, and I think is a nice thing for patients to have accessible to them.

Andrew Schorr:
Mm-hmm. So, Dr. Johnson, as president of ASCO now, you have thousands of members around the world, and certainly around the U.S. And many of these are community oncologists who are dealing with the change in cancer in all these subtypes. If we had 50 cancers or 25 cancers, now we have 2,500, it almost seems, or a lot when you rattle off all these genes. So what advice would you give patients today, wherever they may be, so that they get this changing science and hot it applies to them? What advice would you give?

Dr. Johnson:
Well, I think—let me deal first with the docs. One of the things that we will be working with ASCO, and one of the things that we do in the Boston area and around New England is trying to make additional resources available to the docs, both in guidance about how and when to do both tumor testing, as well as what has been called liquid biopsies or testing of the blood.

And the second thing is that we are trying, through pathways and through other prompts, to help inform physicians about the latest drugs. So, for instance, at our latest meeting at ASCO, it looks like the drug of choice for the first-line therapy of ALK rearranged tumors that we've heard Matt Ellefson talk about is a new drug called alectinib (Alecensa). And one of the things we think is within our electronic medical record, you should have a prompt saying that it's electronically populated that if you put in that the person has an ALK rearrangement, that you try to order Xalkori or (crizotinib) that you get a prompt to say, well, this publication—this was published simultaneously in the New England Journal at the same time—that you'll have a prompt to the physician to inform him that there's a new agent of choice for this agent.

And have it embedded within the electronic medical record. So, that's the first thing. The second thing is that you ask about getting second opinions, and what should the patients know? The first thing is that—and one of the things that we do at our center is we offer second opinions. I do a lot of them. And the vast majority of people go back to their community oncologists. And that's one of the reasons we stay in business. We say, well, we agree with what the doc's doing. But if your tumor grows—because whatever they're getting is working, we tell them, if the tumor grows, come back and see us. And the docs are pretty good about working with us, send them in. About the remote consultations, we do offer a service here.

It's the Dana Farber Grand Rounds. And it's www.grandrounds.com/danafarber. Now, I don't know about Dr. Spira, but I myself, I don't do them. I don't like the—I'm not very comfortable dealing with video. I've done video consultations with two established patients over the course of 10 years, because I think it's very difficult for the communication. Now, other docs are very comfortable with it, and other patients are very comfortable with it. But we do think it's important for people who either don't have the means or the time to travel, that people can access these second opinions using web-based technologies.

Andrew Schorr:
Okay. So, I want Matt—so, when you hear this, you feel that there's a lot of power for patients.

People are terrified when they're first diagnosed. The family's so worried about it. Do you feel that—it takes a lot of courage to ask questions when you go before one of these doctors. But it sounds like you really encourage that in people. Have a dialogue and get informed.

Matt Ellefson:
You're absolutely right, Andrew. And it is—it's a time in your life where—for most people, this is the worst thing that's ever happened to them in their life. And it doesn't only happen to us, to the patient. It happens to our entire family. Our entire family, our friends, our whole social network of people have been impacted in a major, major way. And we don't know what to do. I mean, nobody ever thinks cancer's gonna happen to them. That's something that happens to other people, or that's what we all think. We feel bad about it, but we don't ever anticipate that we're gonna receive a diagnosis someday, so we don't go around studying what should we do when we get cancer?

So when we receive a diagnosis, we're uneducated. We're unprepared. We don't know what to do. Our world comes crashing down on us. Not just in our own mind, but everybody around us is also stressed out and emotional about it, which really adds to it even more significantly. And you really need—you look to a friend in your oncologist. You don't want to also challenge him or her, because you're already in a big challenge. So, oftentimes, patients are just nodding their head, yeah, yeah, let's get going. Let's get started. And to be honest, sometimes that can be the worst thing to do, because sometimes you need to be patient and make sure that all of the testing is being performed, and all of the upfront diagnostics are being performed first before you can really establish what is the best treatment strategy for me?

And that is difficult to do when you're a patient, to have that level of patience. But I was told by my doctors initially, when I went for a second opinion, to feel free to think about it. Two weeks is not gonna make a difference but don't take a month. Make sure you're comfortable. If you want a third opinion, go do that. But make sure you really understand all of your options. And I would echo that to every patient out there, that it's really important that you understand what your options are.

Andrew Schorr:
Mm-hmm. And I want to remind you that you can send questions to Don at questions@patientpower.info. And Don, you're gonna start firing them in a minute. Dr. Spira, I wanted to ask you something.

I mean, you don't have your white coat on today, but I see it on the chair. But you can see how daunting it is if I come see you, or I'm referred to you, and I'm terrified. I've been diagnosed with lung cancer. There's my wife, maybe my kids. We feel—maybe we've lost people, friends, neighbors who've died in short order of lung cancer. We're terrified. Do you welcome questions? Do you welcome a partnership? And as you begin to talk about trials and we're answering questions that sometimes are not answered yet, how do you feel about that dialogue?

Dr. Spira:
You can't be an oncologist in this day and age and not welcome that dialogue. I mean, patients are educated consumers. The Internet is a good thing. There's a lot of information out there. So you have to be willing to listen to the dialogue. I find it all very helpful. Lung cancer, since that's what we're talking about today, is complicated. It's no more two diseases. It's 10 diseases.

So somebody that comes in and already knows about the basic questions to ask—which mutations, why are we doing this, has read about it or seen the ads on TV—for the immunotherapy, these are all great questions, and you have to be willing to answer those questions and have a dialogue with your patients, and have a good relationship with them. So, yeah, absolutely, you have to want it, and that's part of the job.

Andrew Schorr:
Mm. Don, I want to ask you, because I've been seeing you on my screen nodding your head along the way. Matt said things, the doctors have said things. For you, getting a second opinion, having an active dialogue with your doctor, considering clinical trials, knowing—having the right tests, all this resonates with you?

Don Stranathan:
Yes, Andrew. And I also work with people that are newly diagnosed. And I tell them to ask questions. Matt has an excellent 21 questions on the SURVIVEiT website. I usually point that out to them.

And I also tell them, if they're not on social media, find a family member that can be their social media ambassador and reach out. I connect them to the different groups where they can ask questions, find out about side effects. But yes, when I was stable on erlotinib (Tarceva) for six years. But every time I'd go in there, I'd ask my oncologist, "Well, if I wasn't, if the scan wasn't stable, where would we go from here?" And I've done that over the last eight years. And when I did have progression in 2015, the first thing I did—and my oncologist was fine with it—I reached out to an oncologist at Next General for a second opinion, and ran it all by my oncologist, and they both agreed. But I think getting second opinions are important and testing. If you don't know what's driving your cancer, you don't know how to treat it.

And I think, like Matt said, you need to take a little time. Because people panic, and I did myself. Immediately, I wanted to get into treatment and deal with the cancer and get it out of me. But in hindsight, I look back, and even though I've been I think what they call a super responder—I've done very well on targeted therapy, and now on immunotherapy. But I tell people, slow down, take a breath, and ask questions. Because you don't know what you don't know.

Andrew Schorr:
Well, you're super in my book, Don. Thank you for that comment. Dr. Johnson, I just want to go back for a second about testing for a wider array of these mutations. So Don and I have a friend in California, Lisa Goldman, who was initially tested just for one mutation, EGFR, that you mentioned. And you were very involved in it. And then fortunately, with the help of one of the foundations, the Bonnie Addario Lung Cancer Foundation, she then was able to get a broader group of testing.

And what popped up is one of these more rare ones, ROS1. And there's been a medicine that she's been getting that's helped with that. So, if I read you right, it sounds like a broader panel of testing is a good thing.

Dr. Johnson:
As I mentioned before, there are four that have approved drugs. And it turns out the cost of getting a broad panel is not very different than what it would cost to charge for each individual test. And one of the things we've negotiated, and not just us, but other major medical centers here in the Boston area, is negotiate with some of the payers. And Medicare also

covers panel testing now. And it's a challenge to get the insurance companies to pay for it. But so far, and but for us, as a major cancer center, we subsidize the cost of doing it if somebody already has some testing.

So, for instance, the—and this actually happened this week. I had somebody that had an EGFR mutation test and an ALK test in Hong Kong. And I wanted to get broad panel on him, even though he was positive for an EFGR mutation. And one of the things we do is that through philanthropy, we cover the cost, and we can order the same test that we would do in a large panel through a research fund that covers the costs. So we get them on everybody, whether we can charge people for it or not, because we think it's critical to the management of the patients.

Andrew Schorr:
So now we've got to get that going in wider places. So, Dr. Spira, I imagine there have been fights with the insurance companies, right, on some of this. I mean, are you feeling positive that these, we can get more payment for these very informative tests to help more people?

Dr. Spira:
Yeah, there's fights with the insurance company. We've been dealing with that for a long time. And the payment has gotten better. It's not 100 percent uniform. But I think by and large, through efforts like Dr. Johnson's, and there are a lot of companies that are now doing it still, and are very willing to negotiate with payers and work with patients, we can get it pretty much on everybody without the patients having to worry about the cost. You've just got to know to ask it. So, that's the good news. So, over the last 12 months, we've gotten it now uniformly. Whenever we can, we have tissue on any newly diagnosed lung patient.

Andrew Schorr:
Wow, that's good news. And I should mention that my wife and I and some other partners helped found something called the Precision Medicine For Me initiative, and that's been very involved, and some of the other advocates. And there are organizations now helping you with even 20 phone lines you can call and speak to a counselor who can help you connect with testing wherever you are.

And then what happens, Dr. Johnson, as this data comes in on patients, more of the lung cancer community, that helps you in research too, in that you begin to get insight, right? From maybe it's de-identified. It's not Mr. Jones and Mrs. Smith. They're getting they're care. But you're pooling the data together to try to move research forward, correct?

Dr. Johnson:
Yeah. Well, one of the things that Dr. Spira brought up is attempting to get reimbursed. And one of the things I was able to work with, we've put together a group of about 14 leading cancer centers across the country and genotyped 1,000 patients, and then attempted to give them the targets for which they were tested for. And we published this in the Journal of the American Medical Association. Mark Chris was the first author; I was the second. And it showed that the people who got the test, and they were tested for ten genes, which is what we were testing for starting back in 2008.

And it showed that the people who got the testing of the targeted agents lived a year longer than the people who were tested and either had a target and didn't get treated, or didn't have a target identified. We're attempting to do a similar analysis of somewhere around 5,000 lung cancer patients that we've treated at our center over the last 13 years. And I actually had a meeting about it today to take a look at what's happened since we first started testing for EGFR in 2004, and look at the numbers of drivers that we find, and how many get targeted therapies, and if the outcomes of our patients are better. Once we generate that data, because the insurance companies are appropriately asking, can you demonstrate that this has an impact on your patients? I think Matt and Don are living proof that it does. But typically, the companies want more than anecdotes. And so, we're working to try to generate this information, working with our outcomes people to show that this is really making a difference.

And I fervently believe it. I've been a believer since we found the first oncogenic driver in 2004, and we started immediately testing people, even though there wasn't a commercial test, and thought it was critically important, and we've expanded it over the years.

Andrew Schorr:
Okay. Well, we're gonna go on to our questions in just a minute, Don. And send them to questions@patientpower.info. So I always like to ask this question, because really, Dr. Spira and Dr. Johnson, you're our barometer for hope, really. So, Dr. Spira, you've been at this for a while. Dr. Johnson, you've been at this a while. In lung cancer, do you have increased hope, based on all the science we're starting to hear about, the genes we're starting to hear about, the immunotherapy we're starting to hear about, and seeing two guys here who are longer term survivors, how do you feel about the pace of change? So, if I were a new patient coming in, you obviously want to look at my situation. But would you be hopeful?

Dr. Spira:
Yeah, I mean, absolutely. I mean, the pace of change has been hard even for those of us who subspecialize and know the field, lung cancer in particular, well, it's still hard to keep up because it's changing rapidly. As you heard from Dr. Johnson before, you're talking about people that are now living three and four years on these immunotherapies. We had the targeted therapy story now for a few years, but now you're having people without these driver mutations living three, four, or five years. And there are some people that use the word "cure." I mean, that's a long stretch. But yeah, we never used to think about that at all. The fact that we're bandying these about and talking about these long-term survivors is almost unheard of. And while still minority patients, we all anticipate it's gonna get better going forward. So, yeah. Absolutely.

Andrew Schorr:
Dr. Johnson, I'll ask your answer, and also whether some of the therapies we have now can be the bridge to what's next.

So for our friend Lisa who's back in California and wondering how long her Xalkori is gonna work for her, might that be a bridge to something that you're gonna have that comes out of the lab?

Dr. Johnson:
I want to make a couple of comments about the great hope. The first is a personal experience. So, as I mentioned, you asked me about small cell lung cancer earlier, and I said that my first paper I ever wrote was on five-year survivors of small cell lung cancer. I work with one of our trainees, Jessica Lynn, and wrote—we wrote a paper on five-year survivors of EGFR lung cancer, which is—and it's about the same proportion. Now, we want to see it become more, but it certainly gives us hope that we can tell people that you have a substantial chance of making it for five years. Now, five years, for us who have worked with this for a long time, they seem pretty long, but not necessarily.

The second point I wanted to make, and I'm looking at trying to do this in one of my patients who I may start on therapy next week, is that one of our principals in cancer treatment is combination therapies. And all of the things that we've been talking about here, and Matt and Don know this, is that we generally give one agent for the targets. The exception of that is for BRAF you give two drugs. You have dabrafenib (Tafinlar) and trametinib (Mekinist), ones that block two different parts of the pathway. But we're now branching out in each of our mutants and doing two agents that block different parts of the pathway. And one of the things that we think, by doing combination therapies, which is one of the principals that we had to do with chemotherapy to cure people, is that we hope to be able to see these when we put together rational combinations.

Andrew Schorr:
Okay. Well, and I get this, that you are hopeful. So if I were your new patient, you'd run a panel on me. And obviously, we'd look at my situation. But would you be encouraging? You're seeing it broadly. Can I see you smile, I guess? Can I see you pat me on the back, and we maybe have some hope?

Dr. Johnson:
So let me tell you one other anecdote that happens. One of the things I greatly admire about Matt and Don is people that get out there and talk about this. And one of the things, we had a very small group of lung cancer survivors when I started up here at Dana Farber 17 years ago. And for those of you who are familiar with Harvard, they have a big saying—have very tub on its own bottom. And it didn't draw a lot of support. And so, we started having receptions at my home. We have a home in Brookline, Massachusetts that will hold a lot of people.

So it was pretty slim. It was 20 to 30 people when we started. But now it's—once a year, we have about 80 to 100 people at my home, and we show the latest cancer research. And one of the things I'm unthinkably proud of is that you can't tell who the patients are compared to the family members. You look at it, and you can't tell. And it's because the treatments have

got it so that people can live with them, and live—we've heard that there are side effects to what people are getting. But people can live a relatively normal life with what we're doing now. And for that, I'm unthinkably proud. And I'm so happy for the folks that do this. And one of the first ladies I started treating once we knew about the mutations is still going almost 12 years later. And she was one of the ones I was able to put on a combination EGFR inhibitor plus another one. And having people that are making it more than a decade from when we first observed this was something that just didn't happen.

It was unheard of trying to do this a decade-and-a-half ago.

Andrew Schorr:
Wow. Well, we're gonna start with your questions, and I just want to make a comment. And I'm not part of the lung cancer community—I'm not part of the cancer community. But just listening to Dr. Spira and Dr. Johnson—Matt, I think you said it earlier. Gentlemen, just thank you and your peers for all you do, and all the people in labs, and the people that participate in clinical trials, for really leading to encouragement in increased survival, for not everybody, but more and more people. Thank you so much. Okay, Don. You are on, so let's start with the questions. You got a good one?

Don Stranathan:
Yes, Andrew, thank you. There's a number—I want to thank everybody that sent in questions. We have about 20 of them so far, and only a couple are directed specifically to Dr. Johnson or Dr. Spira.

So if I pose a question, it's usually to the general panel, but I'll let you know if somebody asks it directed to Dr. Johnson or Spira. The first question—and I'm gonna take them as they just came in, because those people I know are definitely here on the call. The question's from Karen for the panel. We've been talking a lot about precision medicine and knowing your driver genes. There remains a lot of us who have no known drivers, even after testing. What do the doctors recommend to us, and how do they determine the best course of treatment for us? What kinds of clinical trials are available to patients in these circumstances?

Andrew Schorr:
Dr. Spira, do you want to start with that one?

Dr. Spira:
Sure. We all get excited about these driver mutations, the ones we know about, the ones that are still evolving. It's still a large majority of patients will not be eligible for those, just because they're—at most, they make up about 40 percent of patients, looking at all of them.

What you want to be asking is, am I a candidate for immunotherapy? You want to be asking about what's called your PDL status. We all hope, by the way, there's gonna be a better test for that than we are using currently in the next few years. If you're interested in a clinical study, you want to ask, is there one for me? Is it convenient? Do I want to do it? How much more time is it going to involve? What are the risks? I personally think everyone should be asking for a clinical study. At the best we have, our treatments are still not good enough. So, if there's something that makes sense, yeah, you want to be asking about participating in it. Many of our patients still get chemo. Chemo's gotten a little bit of short shrift, but in all oncology practices, most of our patients still will be getting chemotherapy now and for the foreseeable future as well, and there's nothing wrong with it. Chemo by itself has actually gotten a lot easier as well. So don't be discouraged, disappointed, angry or anything. Just make the best of it that you can. And again, if there's a clinical trial, ask about it.

Andrew Schorr:
Dr. Johnson, your comment when no gene seems to be observable?

Dr. Johnson:
The stuff I have to add to what Dr. Spira said is—number one is, I think you have to be mindful that there's no identified oncogenic driver, or there's no driver mutation that we discovered that we have a drug for at this time. And as Dr. Spira said, chemotherapy is effective, and a number of our patients have lived long enough on conventional treatment that there's enough scientific progress that an effective drug is discovered for the driver. So, for instance, at this year's ASCO meeting, there's a new one that takes place on lung cancer in a percenter cell called MTROK, M-T-R-O-K. And there were

no effective drugs, and it turns out there's a drug made by a company called Wakso that works in 75 percent of the tumors. So that was something that we didn't know until this meeting.

And so, I'd like to emphasize that just because you don't have one at the time you're diagnosed doesn't mean it won't become available when we use other treatments. The second thing is that—and one of the things I try to do is that, as Dr. Spira mentioned, you want to have the PDL1 testing, because some of the people can get treated with immunotherapy. The other thing I try to do with almost all my patients who don't have an identifiable driver is to put them on combination immunotherapy agents. There are classes of agents called IDO inhibitors, and there's other DNA modifying genes that we try to do where we think it's gonna be active in ones that we aren't 100 percent confident that a single agent's gonna be real healthy.

Andrew Schorr:
Okay. Thank you. Don, got another one?

Don Stranathan:
Yes. Nicole asked about EGFR mutations for people. Is there any new research or clinical trials through EGFR?

Former smoker, and she's heard that the immunotherapies don't work as well for people that have the driver mutation EGFR.

Andrew Schorr:
Hmm. Dr. Johnson, you talked about that a little bit when you were talking about smokers before. So, can immunotherapy work, but if you also have EGFR?

Dr. Johnson:
Well, I think Dr. Spira mentioned before, the three approved agents for EGFR mutations at the current—as initial therapy are pembrolizumab (Keytruda) and afatinib (Gilotrif). Those are the three agents. And as Dr. Spira mentioned before, when those quit working, the most common reason they quit working is they get something that you can pick 75 percent of the time in the blood, and the rest of the times, in the tissue, they get something called a T79DM mutation. In that group, there's a second drug called osimertinib (Tagrisso).

Now, one of the things that people are attempting to do now is putting together combinations of EGFR inhibitors. And the two leading candidates of giving combinations are including a class of drugs called MEK inhibitors and MET inhibitors, with the hopes that they'll work longer. The other thing is, this year's ASCO meeting, there was a new drug called dacomitinib that looks like it may work about 50 percent longer than one of the approved agents, afatinib. And we'll be looking to see if that's gonna break into this initial therapy more frequently, given that it's a bit more side effects, but it looks like it may be more effective. So, that was a new event at ASCO this year, and it's a drug made by Pfizer.

Andrew Schorr:
Wow. So, Dr. Spira, as we hear about this, I mean, it sounds like alphabet soup to us patients. Very complicated and changing, happily at a pretty good rate.

Are the guidelines changing too, so that wherever you go to the doctor, you can get a second opinion, but that there's greater understanding of how this changing landscape could apply to me?

Dr. Spira:
Yeah. I mean, the guidelines are changing. As soon as something happens, the guidelines change, where appropriate, pretty rapidly. Everybody's got a desire to get the best drugs out to patients. So the guidelines do change, and they do adapt pretty darn quickly where we can. So everybody's pretty much on top of everything. You're right, it is alphabet soup, though. And you tell a patient they have cancer and they're progressing, they don't hear the next five sentences you've said. So, take notes, write stuff down, and go to one of these advocacy groups, whichever one it is. There's a lot of good information that anybody can read out there, and take doctor speak and alphabet soup and really drum it down for those times when you're just not able to grasp it all.

Andrew Schorr:
Right. I want to ask Matt for a pointer about that. How have you and your family—you've got five kids, and they all worry about you and your wife, Melissa, I think?

Matt Ellefson:
Yes.

Andrew Schorr:
So how have you demystified this? Now you've been at this several years. Dr. Johnson and Dr. Spira are scientists, really, and they're mentioning all these things. It's hard to keep straight. So, how can a family try to get ahold of it, if you will?

Matt Ellefson:
That's a great question. The number one thing, our family has very strong faith, and that really carries us through a lot of things in a big, big way. But also, what I do, and I recommend other patients to do, is I always want to think beyond my current situation and find out what my next options are so I have that plan B in my back pocket at all times. And I don't give up looking until I find that plan B.

Even though I could be NED at the time, which I was for quite a while…

Andrew Schorr:
No evidence.

Matt Ellefson:
Yeah, no evidence of disease under crizotinib (Xalkori), I was still looking and following and seeing, okay, what's next? Because I knew there would be a day where I'm gonna develop resistance. And so, I would encourage everyone to—you never stop looking at what your next option's gonna be. Follow close enough attention, either by joining an advocacy group—I love what Don had mentioned. There's several social media groups. SURVIVEiT has SURVIVEiT Lung Group that has about 500 survivors on there right now. New patients come on and ask questions, and survivors provide their experience to them. It's just a great way to learn, because it's really difficult.

Dr. Johnson and Dr. Spira both know that they have limited time to educate those patients. And 20 hours in their office, or 30 minutes, or whatever—I mean 20 minutes, not 20 hours—20 or 30 minutes in their office isn't enough time to go through your scans and all your test results, and then also educate what's coming down the line that you should be looking out for. And so, oftentimes, you can get a lot of great information from other survivors that have been down that road and are a little bit farther down the road than you currently are.

Andrew Schorr:
Right. I just want to mention this. You are not alone when it comes to lung cancer. There's Matt, our friend Nicole Russell in North Carolina. Don refers to you as the Godfather among patients. Janet Freeman-Daily and some of the other folks have the lung cancer social media group.

There's ROS1 group, there are EGFR groups, there are other groups. Get connected. Now, that doesn't mean that other person's situation is exactly yours. So you want to check with the medical team and really apply it to you. But there's a lot of support that you can get. Okay, Don, let's go to another question.

Don Stranathan:
Okay. We've covered this quite a bit, but Lisa asked—she's EGFR, has exhausted all of her targeted therapies. She's asking if immunotherapy should be her next consideration.

Andrew Schorr:
Mm. Dr. Johnson?

Dr. Johnson:
I think one of the things that we've heard before is that it turns out, if you have had an EGFR or an ALK rearrangement, the two most common drivers in lung cancer, immunotherapy taken in its totality is less likely to work than those that have a squamous cell lung cancer once it doesn't have the drivers.

That said—and Don, you're living proof that there is a subset of people that respond to them. And one of the things at the current time is that I try to get almost all my patients on immunotherapy at one time or another, with the idea being, is that of the treatments that we have available, it's one of the few where you have some kind of confidence, or maybe, albeit small, but a chance that they'll be alive and have their cancer controlled for years. So even though some of these EGRF are mutant positive, and the odds are not as high as you'd like, I still do what your doc did, and that is to get people a shot at the immunotherapy agents and check what works.

Andrew Schorr:
Mm-hmm. Dr. Spira, you too. And I know there are more and more of these immunotherapies. I don't know if they're all equal, but a lot of companies are working on it.

So, this strategy, if the EGFR medicines are sort of pooping out, if you will, that immunotherapy might be worth a try?

Dr. Spira:
Yeah, so, you almost never say never. I think we can all give you the example, and I think as Dr. Johnson said, Don is the greatest example there. I told one patient it was unlikely to work, and lo and behold, she's been on it for seven months so far. And that's a lot more than I would have thought. I also do think it's a prime situation if you have an easily available or a semi-easily available clinical study. We do know that the standard checkpoint inhibitors don't work very well. So, if you're willing and game, it's a good chance to try one of these new combinations or new immuno-oncology drugs, because you're a prime setup for that as well.

Andrew Schorr:
Yeah, I will say, just meeting people at ASCO, gentlemen, there are a lot of companies working on this. And I know you all do the trials. But there are a lot. So, the ones you see on TV, and there are others coming, and there's a lot of work going on here. Okay, Don. So, Don, let's get another question.

Don Stranathan:
Okay. This question is from Nisha. She's EGFR. She says she's on a clinical trial for Tarceva. She had testing, and the testing was positive for T790. And what she's asking, she says she doesn't have progression yet on Tarceva. And since Tarceva only works, she feels, 11 to 12 months, should she stay in Tarceva or switch? And I was wondering—I didn't think you could get T790 unless you already had the...

Andrew Schorr:
Mm-hmm. So, Dr. Spira, you'd better tell us what T790 is, and then maybe you can help answer that.

Dr. Spira:
So, T790M is a mutation one can get. The typical pattern of what you do is you follow somebody till it's not working. Usually, you get a scan. The first line therapy here, and Tarceva's not working, you get a scan, you're gonna get a biopsy, you get a blood test, then you find the T790M.

There's a lot of interest now in finding these mutations a little bit early. Certainly, you can detect T790M in the blood probably before you even have progression on imaging. Knowing that the reason T790M is present, it basically prevents first-line drugs, afatinib (Gilotrif) or erlotinib (Tarceva) and gefitinib (Iressa) from working. If I had T790M at that point, despite having radiographic progression, I probably would switch, only because you can make a pretty sure guess that it's not gonna work fairly soon. If your oncologist decides not to, it's not wrong, but I would anticipate needing to switch pretty soon. They're actually doing a couple of studies looking at osimertinib (Tagrisso) in the first-line setting to see if you can get prolonged survival. And they actually have seen, preliminarily, some good outcomes. So, again, the caveat's an individual test, but if I had it, I probably would plan on switching now, or you're likely gonna switch soon regardless.

Andrew Schorr:
Mm-hmm. Dr. Johnson, any comment from you about—it's kind of like when to switch?

Dr. Johnson:
We've been working on doing blood tests on our patients, and this is led by Jeff Oxnard, and one of the members of our group, and Adrian Satcher published something in the Gem Oncology. And one of the things that happens is you can pick it up in the blood on average of about two months before you see radiographic progression. And when I say you pick it up in the blood, that's what Dr. Spira talked about, this T790M, which is a mutation that arises in people exposed to this class of drugs that inhibit the epidermal growth hacking cell. In general, we wait until we get radiographic evidence of progression.

And one of the things we've also done some research on—and I don't know what Matt's and what Don's experience is—but one of the things we always say is slow progression in lung cancer's not necessarily bad. And there's quite a bit of research to show that people can remain asymptomatic for an average of four months from when you can first see it start to grow, and lots of the trials have built that in. So I'm one that waits a while until it starts showing up. The other caveat I always say, and I won't speak for Dr. Spira. One of the caveats I always try to say is that when people ask us about a specific medical condition, this isn't really a very good venue to offer medical advice. So, we're saying in general how we would approach this.

Andrew Schorr:
Right.

Dr. Johnson:
But when we say this, you can go and discuss it with your doc. But what we're saying is this is how we generally handle it if we were seeing somebody in our practice.

Andrew Schorr:
Of course, of course, yeah. Let me just reaffirm that.

So folks are sending in some pretty questions. What should I do? And again, you're gonna need to sit across from your doctor who you have faith in, or if you seek a second opinion, and say, "Let's look at my situation. What would you recommend?" And in the end, it's gonna be your decision. But it's difficult for Dr. Johnson or Dr. Spira to really say do this or do that just based on their Internet conversation. Don, go ahead. What's another one?

Don Stranathan:
Question's from Peggy. She said, "Great strides have been made in targeted therapies and immunotherapies for people that expressed PDL1." Her question is, for people that have a low-term tumor burden and don't have driver mutations, is chemotherapy the only option?

Andrew Schorr:
Okay. Dr. Spira, you talked about that. You talked about chemotherapy.

Dr. Spira:
Yeah. I mean, so chemotherapy has gotten a little short shrift, because it's not new. It's old. But yeah, chemotherapy, as I said, still works.

And we still use it. There's some new data whether or not you should be combining with immunotherapy in all comers. It's actually interesting, and there's still not an answer despite some wonderful data and even FDA approvals. That being said, chemo is still what we give to most of our patients. And chemo works. And chemo's not as toxic as it used to be. It does have a bad rap, but that's what the backbone of our treatments have been for a long time, and although less, still probably makes up the majority, or at least 50 percent of our patients. And it's not a bad thing. You should not feel bad. You should not feel upset. Patients coming in that are smart that have read, they want a driver mutation, or they want high PDL status. And if you get neither, they are disappointed, for obvious reasons. You can't change it, but you shouldn't be upset. You should just deal with it as a problem and hope that chemo's gonna work for you.

Andrew Schorr:
Mm-hmm. Your comment, Dr. Johnson?

Dr. Johnson:
Well, number one is I agree with what Dr. Spira said. The thing I want to emphasize is that a lot of these classes of immunotherapy drugs are approved whether you do or do not have evidence of PDL1. So nivolumab (Opdivo) and another drug called atezolizumab (Tecentriq) are both approved without the presence of the PDL1. So we mentioned before that at some point, and as Dr. Spira mentioned, the first line of therapy in this setting should be—in general, we approach this and give chemotherapy. But there are people who test negative for that test that we've talked about, the predictive test for PDL1, who still respond and can respond for a long time. It's less than if you have the marker, but it's a subset. So, we think chemotherapy first, but keep in mind that immunotherapy and the second line, after you've had one treatment, is the agent of choice at the current time, even if you're PDL1 negative.

Andrew Schorr:
Okay. Don, let's see if we can get to another one.

Don Stranathan:
Okay. This question is from Byron. Byron was EGFR, non-small cell lung cancer. He had been on a targeted therapy, Tarceva, and then his cancer mutated to small cell lung cancer. He had the spot radiated. He's asking, even after the radiation for the spot for small cell, should he continue to stay on a targeted therapy like Tarceva?

Andrew Schorr:
Hmm. Dr. Johnson, you were kind of nodding your head. It sounds like you've seen that change from non-small cell to small cell. But what should he do?

Dr. Johnson:
Well, first of all, what ends up happening is that—and one of the things that we talked about before is that they've done those studies that were published a couple years ago that defined the genetic changes in small cell lung cancer. And one of the ones that you can't target but is real consistent is loss of a gene called retinoblastoma.

It's a gene that was originally observed to be mutated in kids that got a cancer in their eyes. And it was one of the first inherited cancer syndromes discovered. So, it turns out that that genetic change in small cell also takes place after you put this under the selective pressure of an EGFR inhibitor. What one generally does if it's the—and once again, I'm saying this as a general approach—if there's only one spot that you can find, and you treat it locally, and there's no other small cell evident, you can keep the EGFR inhibitor going. If there's small cell that's disseminated, we usually switch to chemotherapy and attempt to treat them with a small cell-like regimen.

Andrew Schorr:
Right, great. I want to take one more, Don, and then we're gonna get some final comments from everyone. I just want to also plug the fact that we at Patient Power, and working with SURVIVEiT and some of the other organizations have been working hard to interview a lot of experts—Dr. Spira's been on programs before.

Dr. Johnson's been on programs. I want to mention, look at the totality, not just what we are doing today. And we hope to do more. But take a look at a program we did from ASCO with Dr. George Simon from MD Anderson; Dr. David Carbone from Ohio State. There have been other interviews with a number of advocates, some of the European doctors as well. So, resources to look at—our number, including patientpower.info, and also look at the Precision Medicine For Me website we set up, which is precision-medicine.me. And you can see a lot of programs there, including some of the leaders from some of the advocacy organizations who are very devoted to you, as Matt is today with SURVIVEiT. Okay, let's take one more, Don.

Don Stranathan:
Thank you, Andrew. This question is from Leanne. It's a two-part question.

First, she wanted to know what new promising research is being done on small cell lung cancer. And then if somebody could comment, is there any promising treatment for TP53 indication?

Andrew Schorr:
Okay, who wants to do that? Dr. Spira, any comment about that?

Dr. Spira:
Sure. And I think Dr. Johnson mentioned it a little before. So, small cell's been a tough disease. We haven't had a lot of new drugs approved. There's only been one drug approved in about 25 years. However, there's probably headway in a couple of things this year. I mean, you heard about Robate, which is a completely new mechanism of action. It's an antibody drug conjugate, and Dr. Johnson talked about it before. And there actually is some data for immunotherapy as well. So, I think for the first time, we do have a couple promising things. I think you could probably make a safe bet that something's gonna get approved, probably in the next 12 to 24 months.

So, there is, for the first time in a long time, a little excitement. In terms of P53, there are a few drugs in development right now. We're looking at things that have worked with DNA repair, perhaps in combination with chemotherapy. We actually were participating in the study as well. But P53 has been a challenge for a long time, and it's unclear how much headway we're gonna make. But people are studying it.

Andrew Schorr:
Well, I think the news is very positive. Dr. Johnson, any comment about that P53?

Dr. Johnson:
Well, P53 has been around a long time. It's been known to be mutated in lung cancer for more than 30 years. I mentioned before the retinoblastoma gene that when it's mutated when you get small cell, like from the EGFR mutant lung cancer. It's from a class of drugs called tumor suppressors, which are ones that are important for the development of cancer, but are very difficult to target. And at least in my opinion, so far, the ones that are directed against P53 are not our most promising avenue of research, but stay tuned.

Andrew Schorr:
Okay. Well, I think that's the message overall, is really stay tuned. Have hope. And I know that—I don't mean to be trite about it, but we've covered a lot in these 90 minutes. And so, I really want to thank the doctors for being with us. Dr. Spira, from Virginia Cancer Specialists. Dr. Bruce Johnson from Harvard and Dana Farber, and your leadership in ASCO, and helping this knowledge proliferate throughout ASCO. And your leadership within the US Oncology Network in Virginia Cancer Specialists, Dr. Spira. Don, I want to thank you and wish you well with all you're doing, and thank you so much for being here. And Matt, I guess a final word from you, okay? You've been listening. Thank you to SURVIVEiT and your leadership in this as well. What do you want to leave people with?

Matt Ellefson:
Yeah. I would like to first thank Dr. Spira and Dr. Johnson for their great work that they're doing, and the colleagues that they work alongside every day, because that provides people like me and Don and the rest of the people that are watching today—it provides us with hope.

And without hope, we don't have much, you know? We just don't have much. And as we hear about the level of passion that both of you have brought to this webinar today, and that you bring to the rest of the industry when you go out and talk, we can't be more thankful. I just don't know how to express that in a bigger and deeper way. And I just—I feel very fortunate to be the beneficiary of some of your research and some of your colleagues' research. And I want to leave it with—I want everyone to know that there is hope. And I want people to know that you can have the same opportunity that I've had. You can take this initial diagnosis of living eight months and turn it into working on to eight years.

And there's nothing secret about me living in Sioux Falls, South Dakota being able to do that. It's just getting to the right place, getting to the right people, doing the right things at the right time. And this webinar is providing you with just a wealth of information. Continue to look, continue to be thankful for what you have, and don't ever lose hope.

Andrew Schorr:
Amen. Thank you so much for those comments. Thanks to our whole team, our producer, Tamara Laban Jones, the team at Virginia Cancer Specialists and Dana Farber, and ASCO, who've worked with us and the SURVIVEiT, of course, your organization, Matt. And thank you to you and Joy. Well, we hope to have future programs. But remember, the replay will be available soon. There's a survey that we will be sending you via email.

We'll send you the links to that, to all the resources we said we'd put together, the glossary, the start here graphic, the questions to ask your doctor, remote second opinions—to what degree that makes sense to you and your doctor, and also, the patient guide that we were very grateful to Foundation Medicine for providing us. And I want to thank our sponsors, Celgene, AbbVie, Foundation Medicine, Novartis, and Garden Health, and also additional support from Vivify. They're all working together from different directions. Drug companies, diagnostic companies, decision support groups help you and your doctor. And we didn't have all this to talk about not so long ago, and now we have a lot more. So, signing off from Philadelphia for the folks in Virginia, and Boston, and Sioux Falls, South Dakota, and California, I'm Andrew Schorr. Remember, knowledge can be the best medicine of all. Thanks for joining us.