



ROS1 Positive Lung Cancer: Managing Resistance and Advancing Research Transcript

Diane Mulligan:

The composition of each person's lung cancer is unique, which makes identifying a biomarker so critical. It allows for targeted treatment. Hi there, I'm Diane Mulligan.

Jordan Sherman:

And I'm Jordan Sherman. ROS1-positive is a biomarker which can drive the growth of a cancer tumor. But thanks to research, we now have precision medicine that combats that growth.

Diane Mulligan:

So ROS1 is our topic today on Lung Cancer Foundation of America's, Hope With Answers podcast.

Dr. Tejas Patil:

There is a lot of important research going on in ROS1 non-small-cell lung cancer. One of the hot topics in ROS1 lung cancer is, how do you manage resistance to the ROS1-targeted therapies? And for that there are many drugs in development that are currently being studied in clinical trials.

Lysa Buonanno:

I was actually excited that there was a clinical trial available for me to join at the time when I needed it. I feel like it's my opportunity to give back and help, and contribute to research to further treatments for this disease.

Diane Mulligan:

Lung cancer is a tough topic. It's a disease that affects patients, families, friends, coworkers. But first, it's a disease that affects people. The Hope With Answers Living With Cancer podcast brings you stories about people living, truly living with lung cancer, the researchers dedicated to finding new breakthrough treatments and others who are working to bring hope into the lung cancer experience.

Jordan Sherman:

We are recording this Hope With Answers podcast in November of 2023, the very month the U.S. Food and Drug Administration approved a new drug for ROS1-positive lung cancer. It's just a simple pill, but Diane, it's showing a lot of promise.

Diane Mulligan:

It is, and it's a testament to research, because you know, Jordan, we have learned more about lung cancer in the past several years than we have in the past 25 years. And

among those benefiting from all of this research are people who are living with ROS1 lung cancer.

Jordan Sherman:

So let's learn a little bit more from our guests. We'll hear from Lysa Buonanno, a patient advocate living in Florida, diagnosed with ROS1 lung cancer. But first, we'll begin with Dr. Tejas Patil, assistant professor of medical oncology at the University of Colorado Anschutz Medical Campus in Denver. Dr. Patil, can you tell us a little bit more? What is ROS1? How do you define it?

Dr. Tejas Patil:

That's a great question. So, ROS1 non-small-cell lung cancer is a mouthful, so let me break it apart. We had the last part, which is non-small-cell lung cancer. And the ROS1 comes from this growing trend in lung cancer where we're going beyond just calling it lung cancer and really getting down to the genetic level.

And so ROS1 is a type of mutation that we see in patients who have lung cancer. It's one of many but it's an important one because there is targeted treatments available to these patients that really are not like chemotherapy. They don't have the same side effects, they're very different. And so that's where the term ROS1 non-small-cell lung cancer comes from. It's just really recognizing the importance of one, doing genetic testing, and two, trying to pair patients with targeted treatments if that's appropriate.

Diane Mulligan:

That's great information, it's so important for patients to really understand. Dr. Patil, I know ROS1 is a very aggressive type of non-small-cell lung cancer and it can spread to the brain and the bones. It is one of more than a dozen types of lung cancer that we know about now. Why is it so important for people to ask, "What is my biomarker?"

Dr. Tejas Patil:

That is a fantastic question. And let me start by saying that lung cancer generally is quite aggressive. So if you just never did any biomarker testing, we would find patients where lung cancer has spread to the brain and to the bone. But what is important about this biomarker-testing question that you've asked is really the fact that it allows patients the type of treatment that they normally wouldn't get if they didn't have this test.

So really, what you're telling a patient when you say, "You need to get biomarker testing," is "The genetic makeup of your tumor, you need to understand that so that we can know how to give you the most appropriate targeted treatments." And it's specifically for ROS1, this is important because they are pill-based treatments. These are not chemotherapy, they only work if you have ROS1. If you don't have ROS1 you're not going to have any benefit from these pills. So knowing that is important so that we can prescribe that properly.

Jordan Sherman:

I think that when you hear lung cancer, and especially a lung cancer diagnosis, with it being the deadliest of all major cancers, you have that pit in your stomach, that fear. But we've seen some incredible strides in lung cancer research which helps develop new,

targeted treatments, as you alluded to before. Can you talk a little bit more about why research is so important and funding research is so important, and the continued funding of research is so important for future treatments?

Dr. Tejas Patil:

Very good question. And so, one of the reasons that research is so important in the field of lung cancer is that with research we can offer patients better treatments that improve, not their quantity of life, like how long do they live, but also their quality of life. These two things go hand-in-hand. I'm often thinking of history when I think about the need for research. And 20 years ago we would be having a very different conversation about what lung cancer treatments look like. In fact, the conversation would be very short. It would be, "You have lung cancer. This is chemotherapy, good luck."

Now our conversations are way more complicated because we know that a lot of these patients who have lung cancer have mutations that we can treat with targeted therapies, such as ROS1. But also, the other big player in this space is immune therapy, which I'm not sure if we can go there, if we want to talk about it, but it has also dramatically improved the life of patients.

And so these two treatments, targeted therapy and immune therapy, have really moved the needle such that if you look at the most recent data, the lung cancer overall mortality is actually going down for the first time in 20 years. I think that's in large part due to research that has identified mutations that we can target and also identified the way our immune system can help fight cancer .

Diane Mulligan:

It's so interesting when you talk about the research and the immunotherapy and understanding the biomarkers. This all came out of clinical trial research. So is it still important for patients to consider clinical trial research?

Dr. Tejas Patil:

Absolutely. I'm a big believer that clinical trials are really the way to advance our knowledge in the field. A lot of patients would not benefit from the treatments that they're receiving today had it not been for earlier patients who have enrolled in clinical trials of these same drugs.

What clinical trials do is it offers patients the opportunity to get cutting edge therapy. And one thing that patients often ask me is, "Well, am I just going to get a sugar pill or am I going to get the real drug?" And it is actually unethical to put a patient on a trial where all they're receiving is placebo, unless placebo is truly the best thing you can offer a patient. And that's actually quite rare in the modern era.

So really what trials mean is a patient will either get the best standard-of-care treatment that's available or the best standard-of-care treatment plus some new treatment. And it's really that question that we're trying to tease apart with the clinical trial.

Jordan Sherman:

And from those clinical trials, you get this terminology called precision medicine. Or some people have referred to it as a targeted therapy. And I think that goes back to what you were saying, 20 years ago that conversation would be, "We can give you

chemo but we have no idea how long it's going to work for you." And we know in many cases, at that point in time, it wasn't a very long time at all. So what kind of differences are we talking about here when somebody is able to have a targeted therapy versus a chemotherapy regimen from 20 years ago?

Dr. Tejas Patil:

Right, so targeted therapy has really come out of the recognition that a lot of patients who have lung cancer, their lung cancer actually has very specific mutations. And these mutations cause the cancer to grow and to grow, and to grow. And the recognition of these mutations has led researchers to say, "Hey, what if I stopped that mutation that tells the cancer to keep growing? What happens?" So what happens is when you give targeted therapy, the cancer cell stops growing, it dies. And actually patients do much better on this type of treatment if it's appropriate for them.

The longterm survival for patients who get targeted therapies is oftentimes quite good, often in the order of years. I have several patients in my clinic who are 10 years out from their stage-four lung cancer diagnosis. This is a number that was unheard of 20 years ago. There was basically no one who was alive 10 years ago after their stage-four cancer diagnosis. And so, targeted therapy really remains an important type of treatment in the tool kit that I use as a lung oncologist.

Diane Mulligan:

Dr. Patil, who is eligible for clinical trials and who should be asking their doctor about them?

Dr. Tejas Patil:

So I'm going to answer your last question first, which is that every patient should be asking their doctor about whether a clinical trial is appropriate. Who is eligible is actually very dependent on the trial itself. And each trial has a clinical trial protocol that specifies who can get into the trial and who cannot. And a lot of this is done out of concern for safety.

So for example, if a patient has advanced kidney disease, then the trial may not be appropriate. And that's because we don't know if they're able to clear this experimental medicine through their kidneys because their kidneys aren't working as well. And the clinical trial protocol will say that. So a lot of it depends on the specific trial. But the question should always be asked, "Am I a candidate for a clinical trial?"

Jordan Sherman:

Kind of a double-edged sword when it comes to changing topics really quickly, doctor. It's a double-edged sword when it comes to insurance. Because we know that most lung cancer diagnoses happen when somebody is stage four, unless something else happens and you luck into the diagnosis. And at that point in time you have to go through different paths to get treatment. But there are people who can be screened ahead of time.

Again, those stage-four diagnoses typically come after you start to see some type of symptoms that you might not see in stage one, two and three. So can you talk a little bit about the screening criteria, how most insurance carriers from Medicare to the VA will

pay for those costs if you meet the screening criteria, and who might not be eligible for those?

Dr. Tejas Patil:

Okay, so this is a very good question and this is getting at a very important intervention that we can do as the medical community to help patients not develop lung cancer. And this gets at that concept of lung cancer screening. I mentioned targeted therapy earlier, I mentioned immunotherapy earlier. The other real big advance in terms of reducing mortality from lung cancer has been from lung cancer screening. So I want to really emphasize this as well.

Currently, screening is recommended for patients who have a 20-pack year or more of smoking history, who smoke now or have quit within the last 15 years and are between 50 to 80 years of age. And there has been a big trial that has been done several years ago that show that a low-dose CT scan can help detect lung cancer at an earlier stage, so when it's not spread, when it's not stage four.

Finding lung cancer at these earlier stages can allow patients the opportunity to get treatments that they otherwise may not have been eligible for such as surgery, such as radiation. And this is a very hot topic right now in lung cancer. There is a lot of research going into, how do we take care of patients who have early-stage lung cancer? And so I imagine that in the next two years, if you ask me the same question I'm going to give a very different response.

Diane Mulligan:

Next question I have for you is, what would you say is the newest thing that's going on with ROS1 right now? What's the newest research that's out there that has you excited?

Dr. Tejas Patil:

Oh, boy, how long do you have?

Diane Mulligan:

That's a great answer right there, I love that.

Dr. Tejas Patil:

Yeah. There is a lot of important research going on in ROS1 non-small-cell lung cancer. And I'm going to break it down into two big areas. So, the first area is trying to understand how patients who received ROS1-targeted therapies developed resistance to those therapies. Resistance is a big problem for patients with ROS1 lung cancer. Almost every patient will, at some point, and we don't know how long it is for each patient, it can be 1 year all the way up to 10 years. I have patients who have never progressed from their first targeted therapy, and I have patients who progressed within a year.

But in any event, when they do progress, the question then comes, why did their targeted treatment not work? And what drugs are in development that we can use to help these patients? Most of them are in clinical trials right now. That's one active area of research, what do we do about patients who are progressing on their targeted therapy? The other area of-

Diane Mulligan:

Can I stop you there for one second? Can you define two things, one is, what does resistance mean? And two is, what does progressing mean?

Dr. Tejas Patil:

Oh, thank you, thank you, yes. So, resistance means that the cancer is growing in spite of you taking your medication every day. So for some reason, the cancer has figured out a way around the targeted therapy. And usually this comes in the form of some kind of mutation that evolves as a result of processes that we still are trying to understand.

Progression is a clinical term, and really what that means when the doctor uses it is, they took a look at your scans and there is spots or tumors that they are seeing on their scans that are growing when they shouldn't be growing. That's progression. So one of the hot topics in ROS1 lung cancer is, how do you manage resistance to the ROS1 targeted therapies? And for that, there are many drugs in development that are currently being studied in clinical trials. That's one area.

The second area is a area that I'm very excited about. It's still very much in its infancy, but it's this concept that's very closely related to resistance and it's called persistence. And let me define that. So persistence is this really interested concept which is, when you give a targeted treatment for ROS1 lung cancer, most patients, if you look at 100 patients, most of them are going to have this image on their first scan. So when they come to see a doctor after three months of being on treatment, most patients will notice that something like 60 to 70% of their cancer is gone, it's not there.

But the question that remains is, why is there 30% left behind? It should be 100%. And so this concept of persistence is looking at that 30% that's still in the patient's scan. They're not growing, they haven't developed a resistance, meaning the patient is still on their targeted therapy. It still seems to be working, but for some reason those cells haven't died. And I think that is going to be another major area of research. What is it about those cancer cells that are letting them live or letting them be alive in the presence of targeted treatment?

Diane Mulligan:

Is there anything that we didn't ask you that we should have asked you about ROS1, that you think people out there should know?

Dr. Tejas Patil:

So, ROS1 is a very rare sub-type of cancer. And even though lung cancer is very common, I still think of ROS1 non-small-cell lung cancer as a very niche cancer. And I think it behooves a patient to see a specialist who takes care of a lot of patients with ROS1. The field is constantly dynamic. The treatments are constantly changing and the optimal approach for patients with ROS1 may be changing. And so, that is one recommendation, I would seek a specialist who sees a lot of ROS1 non-small-cell lung cancer.

Diane Mulligan:

It's so exciting to hear the hope in Dr. Patil's voice and see the advancements research is making for those that are living with ROS1 lung cancer.

Jordan Sherman:

And one of the many people is our dear friend, Lysa Buonanno. She, too, is living with lung cancer. Lysa is a Lung Cancer Foundation of America Speaker's Bureau member and a well-known and trusted patient advocate for others facing lung cancer.

Well, Lysa, stop me if you've heard this before, but you don't look like you have lung cancer. Is it difficult when people just don't understand what you're going through and how do you manage those misconceptions?

Lysa Buonanno:

I do get that all the time, actually. And I'm in a good place right now, so that's understandable when you feel healthy and look healthy on the outside. I have had many down, down days and months over these years. But what you can't see on the outside, I'm still dealing with on the inside, not just physically, things that cancer has done to my body, changes that have happened to my body because of it. And also mentally and emotionally you really go through a lot, I think, and the roller coasters of this disease.

So that's not always visible, obviously, on the outside, except for those that are really close to you. And I just take that as an opportunity to explain to them that we're really lucky to have some great treatments right now that allow me to live as close to normal life as I used to before cancer.

Diane Mulligan:

Lysa, the other thing that I think is interesting is that you know your ROS1. How important was it for you to find out that you were? And what kind of difference does it make once you know what that biomarker is?

Lysa Buonanno:

For me it was a game changer, absolutely. You have to remember, when I was diagnosed it was 12 years ago. And biomarker testing wasn't common practice at the time. So I actually didn't know about that driver until 18 months after being diagnosed. And unfortunately, a lot of stage-four patients don't make it through the treatments that I had had at that point.

But I was extremely excited when we found out I had a driver that we knew there was a medication out there to treat already. And that changed my life from doing more chemotherapy and radiation, and possibly another surgery because of tumor locations, to being able to take a targeted therapy made just for that cancer, that helps me live and feel much more energetic, gives me more time and the ability to be able to do other things.

Diane Mulligan:

Now you used the term driver. Can you explain what you mean by that to somebody who is new to lung cancer?

Lysa Buonanno:

So we call these biomarkers or oncogenes or driver mutations. It's really just a gene that's had a little glitch in its replication and it's not behaving the way it's supposed to be. And that's what's driving my cancer to grow.

Diane Mulligan:

All right, thank you.

Jordan Sherman:

I want to talk a little bit more about clinical trials because you talked about how you're on a targeted therapy. And these therapies are developed through clinical trials. So in your experiences, was it difficult to decide to get involved in a clinical trial and what ultimately made you say, "Yes, I want to do this?"

Lysa Buonanno:

I was actually excited that there was a clinical trial available for me to join at the time when I needed it. You hear the term a lot, "You're being a guinea pig. They're just testing that on you." Every single drug that we take has been tested. And that's the only way to find out if it's safe, if it works and I feel like it's my opportunity to give back and help, and to contribute to research to further treatments for this disease. But also, it's a great opportunity for me to be getting the newest and most current, up-to-date treatment that's out there.

Diane Mulligan:

Now if there was one thing that you wanted people to walk away from this interview with, what would that be? And especially for those ROS1ders, as you guys are called out there, what's that one thing that they should know?

Lysa Buonanno:

You have to keep advocating for yourself. Throughout this entire process I think that is so critically important. Educate yourself even a little bit, about your particular disease, so you know what your next options might be, also in case your doctor isn't aware of some of those newer treatments that are out there.

Diane Mulligan:

What a great conversation with LCFA Speaker's Bureau member, Lysa Buonanno, and Dr. Tejas Patil. Not only did they give us great insight into ROS1 lung cancer, but they also provided hope for anyone who is living with lung cancer.

Jordan Sherman:

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Diane Mulligan:

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