Decoding STK11 in Lung Cancer Therapy

Diane Mulligan:

Our DNA is like a highway system. It carries information necessary for our cells to function. But what happens if that roadmap has a glitch or a typo? The cell receives the wrong information signals and that can cause cancer. Hi, I'm Diane Mulligan.

Mitch Jelniker:

And I'm Mitch Jelnicker. Biomarker testing helps to identify those mistakes or typos so doctors can apply targeted therapy. One of the newer biomarkers discovered is called STK11.

Diane Mulligan:

And that's the topic of today's Lung Cancer Foundation of America's Hope with Answers Podcast, STK11 and its impact on those facing non-small cell lung cancer.

Dr. Salman Punekar:

STK11 is kind of a newer kid on the block in terms of a biomarker that we've been considering for lung cancer, but we do think that it's hugely important, especially because it affects the current treatments. It maybe makes the current treatments that we have such as immunotherapy less effective.

Stephanie Williams:

And they are finding that targeted therapy improves disease-free survival. So it reconfirms that I'm on the right track and making the right choices. And I mean in real time clinical trial data is informing doctors and patients on how best to treat our unique cases.

Diane Mulligan:

Lung cancer is a tough topic. It's a disease that affects patients, families, friends, co-workers, but first, it's a disease that affects people.

Mitch Jelniker:

Advances in lung cancer treatments over the last few years have made it possible to live with lung cancer for years after diagnosis.

Diane Mulligan:

The Hope with Answers Living with Lung 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.

Mitch Jelniker:

Welcome to another informative edition of The Hope with Answers Podcast. Our guest today will help explain STK11.

Diane Mulligan:

We'll hear from a patient and a medical oncologist. So let's begin with Dr. Salman Punekar, Assistant Professor of Medicine of Medical Oncology at NYU Langone Health.

Mitch Jelniker:

Dr. Punekar, thank you so much for joining us in joining this discussion with us today. First of all, I got to ask you, how would you define or how do you explain STK11?

Dr. Salman Punekar:

Thank you so much for having me. I'd be happy to talk about this. So STK11 is an area of research that I'm particularly interested in, and so I'd love to share my thoughts on this. So I think it's first helpful to just define what it stands for. So STK11 stands for serine/threonine kinase 11. So that's the STK11, it's often also called LKB1, which stands for liver kinase 1. And these are genes that make proteins that are very important for cells to function normally. It's a gene that's found on the chromosome 19 normally.

Mitch Jelniker:

So would that be a gene that all of us would be carrying?

Dr. Salman Punekar:

Exactly. So everybody has this gene normally, and you'd get it from both your parents. In some cases it can be mutated, and there are two ways they can be mutated. One, it can be mutated in what's called a germline fashion, and that means that it's mutated in a way that your parents can pass it on to your children and then so on and so forth. If you have that mutation in your entire body, that's called a germline mutation, which gives you Peutz-Jeghers syndrome. And then the other way you can get a mutation is if you just have a mutation in a cancer. So if unfortunately you've developed a cancer, your cancer can develop that same mutation and it would be a mutation of the same gene on the same chromosome.

Mitch Jelniker:

What makes STK11 unique?

Dr. Salman Punekar:

So STK11 is what we call a tumor suppressor gene. And so what that means is that in the normal sense, the way it works is that it helps keep cells under control. So cells left unchecked will turn cancerous and will cause all sorts of issues. So STK11's main function is to suppress tumors from arising. And that's a little bit different than some of the other genes that we talk about in cancer, but what makes it particularly unique is that it has effects on a lot of different inner workings of the cancer, mostly within the immune system, and that's the most unique part of it, and that helps drive understanding how it can be affected and what you can do to try to overcome some of the issues with STK11 mutations.

Mitch Jelniker:

Kind of zero in on it. Is it considered a biomarker?

Dr. Salman Punekar:

It is. So a biomarker is just something that you can measure that indicates either a risk of cancer or the occurrence of cancer or how somebody will do. So STK11 is certainly a biomarker. It is definitely a novel biomarker though, so it's something that's only fairly recently been discussed and developed.

Mitch Jelniker:

Okay. Certainly there are different types of lung cancer. Are there different kinds of STK11?

Dr. Salman Punekar:

Yeah. So this is actually the most important thing about STK11 is that in any given gene, and this holds true for any type of mutation, you can have multiple types of mutations. What's key to STK11, I mentioned to you that it's a tumor suppressor gene. So the mutation has to be a loss of function mutation to have an effective STK11 mutation. So that's a little bit different because sometimes you can have STK11 mutations that don't actually render the protein that's developed, and in which case that would be an inconsequential STK11 mutation. So really what we look for is at the end of the day, does this mutation mean that the STK11 protein is non-functional, not doing what it's supposed to do?

Mitch Jelniker:

Right. Yeah. Yeah. Closer zero in on it. Talk about the research being done right now on STK11.

Dr. Salman Punekar:

We do a lot of research on STK11 in two kind of general areas. The first is preclinical research, and what that means is it's mostly lab-based where we're really trying to understand, "Okay, patients who have STK11 mutations, what does that do to cancer? How does that affect the inner workings of the immune cells, the white blood cells, so on and so forth," really understanding the signaling pathways that STK11 can impact. Subsequently, we do animal studies where we look into these things in a little bit more detail. We also then do further studies to determine what treatments might be effective. And that's kind of the whole preclinical side. The other side, which I focus a lot on is on the clinical side. And what that means is that we're actually developing and testing new drugs or assets that might be helpful for patients who have STK11 mutations and giving them to patients, really seeing how they do with it. Does it help their cancer? How easy of a medication is it to take, so on and so forth. So it's really those two big areas of research that we do.

Mitch Jelniker:

And of course, that leads us into the topic. You mentioned the drugs being tested, clinical trials, talk about the importance of clinical trials.

Dr. Salman Punekar:

So from my perspective, as a thoracic oncologist who focuses mostly on clinical trials, it really is something that I think is essential for everybody regardless of walk of life or stage of disease, is to think about a clinical trial because a clinical trial does two things. Number one, obviously it helps improve the knowledge that we have of cancer, and then overall, the more we know about something, the better we can do to help treat it and prevent it, and so on and so forth. But at the same time, clinical trials give patients opportunities to get access to drugs years before they become FDA approved. So that's a very interesting proposition for patients who may have limited options participating in a clinical trial may give them a few more options and hopefully we'll help them do well.

Mitch Jelniker:

And more options in addition to the current standard of care, right?

Dr. Salman Punekar:

Exactly. Yes. So current standard of care should be available wherever somebody goes. And then in general, patients may need to look for clinical trials depending on where they can travel to or what's nearby and so on so forth.

Mitch Jelniker:

Sometimes when we talk to maybe newly diagnosed patients and they say, "Look, I'm a little overwhelmed. I got a lot on my plate at present, and now you're asking me about clinical trials," it might help them to understand what the process is like. What is the patient experience in a clinical trial?

Dr. Salman Punekar:

That's a great question that you asked. So the clinical trials are somewhat of a black box to folks, and I think understanding that really helps. I think that the key is to understand that a clinical trial is really a doctor taking care of you and trying to do the best thing for you as a patient. And that comes down to, in this case, giving you access to the cutting edge of research and technology. So clinical trial is basically somebody comes in, we evaluate them, determine if they're eligible for a clinical trial based on several characteristics, and then not too dissimilar from regular treatments that you would get at any oncologist's office.

We will provide the same type of treatments, maybe additional things, additional testing to ensure that we're understanding how a certain drug or acid is working in a patient and really give you personalized care and keep really close eyes on you because as a patient who has a tough disease, we number one, want to help you as much as possible. And number two, we want to ensure that the medications that we're giving you and actually help you and are safe. Most patients who end up on a clinical trial, it feels almost like you're just being treated by your oncologist. And that's really what it should feel like. For us at an academic center, clinical trials and patient care go hand in hand.

Mitch Jelniker:

Not an added burden for the patient, but an added opportunity perhaps.

Dr. Salman Punekar:

Yeah. Yeah. I always like to look at it as an opportunity.

Mitch Jelniker:

Exactly. And this may seem kind of obvious, but I kind of want to hear it from you that they're in the trenches in this research. What's the payoff of doing all this research?

Dr. Salman Punekar:

So the payoff is huge. If you think about lung cancer, 10, 15 years ago, there were very few options for patients. Now we have innumerable options. I can't even count the number of different therapies that we have that are either in clinical trials currently or are now FDA approved. So all of this happened because of patients participating in clinical trials. They drove discovery, they drove science, and subsequently they drove approvals. And now with those approvals, the standard of care for patients with lung cancer has changed dramatically. In addition to that, the survival of lung cancers is not nearly as bad as it used to be. There's still a lot of work to be done, but we're definitely on the right track in large thanks to all the patients who participated in these clinical trials right from the beginning.

Mitch Jelniker:

Yeah, there's a big payoff for everyone involved. What's the takeaway that we should have about understanding STK11? They all have these acronyms and it starts to sound kind of confusing in medical ease, but what's the takeaway when we're trying to share what STK11 is all about?

Dr. Salman Punekar:

So I think there are two main takeaways. Number one is that you have to know that you have STK11. And what that comes down to is getting the proper testing. So if you never know that you have STK11, you may not understand that it's an opportunity to treat your cancer a little bit differently. And secondarily, it's important to know that generally STK11 mutations happen at the same time as other mutations. And if that's the case, they can sometimes be a predictor of a worse cancer. So knowing where you stand I think is always good. Being fully just transparent and knowing all the information, I think can only put patients in a better position. And then the point after that is this is now information that you can do something about. There are clinical trials, there are new treatment options, there are even other standard of care treatment options. There may be more effective in somebody who has an STK-XI mutation. So all important considerations and things that I really encourage patients to speak with their oncologists about and have really ended open conversations.

Mitch Jelniker:

Yeah, ask about identifying their biomarker, in this case, STK11 then allows for more targeted therapy.

Dr. Salman Punekar:

Exactly. You're exactly right on that. You could only get targeted therapies if you know that you have the target. So that's the key is to ensure that you have had complete biomarker testing, ensure that you know what it means, and so on and so forth.

Mitch Jelniker:

Anything else you'd like to add about this discussion about STK11 that I failed to ask?

Dr. Salman Punekar:

Yeah, I think STK11 is kind of a newer kid on the block in terms of a biomarker that we've been considering for lung cancer. But we do think that it's hugely important, especially because it affects the current treatments and maybe makes the current treatments that we have such as immunotherapy less effective. So I think going forward, our research is really going to focus on how do we reverse that? How do we make STK11 mutations not an additional worst prognostic factor for patients? And that's really what our goal is here when we do this research.

Mitch Jelniker:

Dr. Punekar, great information. We appreciate you taking the time to visit with us today.

Dr. Salman Punekar:

My pleasure. Thank you for having me.

Mitch Jelniker:

It's exciting to see someone on the front lines of battling STK11 so enthusiastic about the progress that's being made and offering more targeted treatment.

Diane Mulligan:

Progress that's thanks to clinical trials and knowing your biomarker. Our next guest is a living example of the advantages of clinical trials and targeted therapy. Stephanie Williams is a member of the Lung Cancer Foundation of America's Speakers Bureau, and a determined advocate for those living with lung cancer. Stephanie, it is so good to see you. We always enjoy talking to you, but for those that don't know you, tell us a little bit about your story.

Stephanie Williams:

I'd be happy to Diane. Thank you. My story with lung cancer started in 2021. I was 37 years old, and I was at a regular appointment with my primary care physician. At this appointment, I brought up to her that I had been experiencing a mild cough for about the last six months or so. It would kind of come and go. It was a little wheezy, but it never bothered me enough to go seek answers or treatment about it. But at this appointment, we decided that I'd have a chest X-ray, and that chest X-ray revealed a mass in my right lung. And over the course of the next month, there was a battery of tests, scans, biopsies, and ultimately I would have two lobes of my right lung removed surgically. And after that surgery, I was staged at 2B, stage 2B non-small cell lung cancer, and I would go on to have four rounds of chemotherapy, and now I'm on a targeted therapy for a planned three years.

Diane Mulligan:

Quite the story. Yeah.

Mitch Jelniker:

Yeah. You hear us all the time at LCFA talk about, "Ask about your biomarker, ask about your biomarker." So I'm sure you did that. How did that question impact your treatment, your journey?

Stephanie Williams:

Well, I was one of the fortunate ones where I didn't have to ask. My surgeon had the foresight to send my tissue for biomarker testing right after surgery. So by the time I met with my oncologist a few weeks later, I knew that I had ALK or ALK positive lung cancer. And because that biomarker was discovered, it's really informed my treatment and affected how I move forward with my care. So I'm so thankful that that was sent for me and tested without me having to seek it. I know many patients, the onus is on them to seek out this treatment or rather this testing that's just so important.

Diane Mulligan:

Steph, I know that you haven't been in a clinical trial, but I think clinical trials are probably pretty important to how you're being treated. Tell us how you feel about all that.

Stephanie Williams:

Well, the ALK positive mutation of my lung cancer makes treatment very interesting because I was staged at an earlier stage, stage two, and there's sort of a new frontier for treating early stage patients. There's not a ton of data or guidelines out there. So when I finished my chemotherapy, there was a big question mark about what we would do next. Thankfully, there was a trial called the ALINA trial that looked at EGFR lung cancer and how early stage EGFR patients are responding to targeted therapy and how that helps them sort of ward off recurrence.

And since ALK behaves similarly to EGFR, we used data from that trial to inform my decision to go on a targeted therapy after chemo, which is sort of beyond the standard of care therapy of just surgery and chemo, and then monitoring. And I mentioned that I'll be on that targeted therapy for a planned three years. I'm about two thirds of the way through now, and I was really pleasantly not surprised, but I received the great information that another clinical trial, the ALINA trial, looked at ALK positive, which is my biomarker, early stage patients getting targeted therapy after surgery. And they are finding that targeted therapy improves disease-free survival. So it reconfirmed that I'm on the right track and making the right choices. And I mean in real time clinical trial data is informing doctors and patients on how best to treat our unique cases.

Mitch Jelniker:

Yes. It sounds like clinical trials have had a positive impact on your journey, even though you've not personally participated in one. I know sometimes when people hear that we're at clinical trial, they think, well, look, I've just been diagnosed. I've got a lot on my plate, and they may not consider it. If a clinical trial arose and it was right for you, would you consider participating?

Stephanie Williams:

I would Mitch. I would consider that right along with standard of care considerations, because like I mentioned, sometimes standard of care just falls short of what patients really want to see for extending our lives. Disease-free survival, overall survival, these abbreviations and terms we get thrown at us quite a bit. And the truth is sometimes what we have right now available to the general patient population just isn't enough. And a clinical trial can offer that hope of the next frontier to us right now.

Diane Mulligan:

Stephanie, I think a lot of people have a lot of misconceptions about what clinical trials are, what kind of care you get, those types of things, and you know a lot of people who are currently on clinical trials. What would you want people to know about clinical trials and what would you want them to consider if they were looking at one?

Stephanie Williams:

Oftentimes, clinical trials are being run by some of the most highly experienced doctors that are regularly treating that type of cancer. So really, you're being watched and treated by, in my opinion, experts in that field. And the monitoring is top-notch. You have eyes on your blood work, your scans, everything. So in a way, it's almost like, I don't want to say more or better, but you don't have to worry that you are not getting excellent care because you will be given standard of care or better with a clinical trial. You are elevated in your monitoring and in your testing.

Mitch Jelniker:

Good point. You've been a very strong advocate for others facing lung cancer and for lung cancer research through a variety of ways, not the least of which is assisting Lung Cancer Foundation of America, but that's not something you have to do. Why is that important for you to do?

Stephanie Williams:

Well, like we mentioned, it's very overwhelming, especially when you're newly diagnosed, to understand this cancer and the many different types, cancer and the treatments. So I want to make sure that newly diagnosed patients are empowered to ask the right questions, questions like, "Has my tumor been tested for a biomarker or mutations," questions like, "Is there a clinical trial that's right for me and my specific needs?" And because there's so much information, those questions aren't always obvious to the newly diagnosed. So that's where patient advocates can come in and reach out and help spread the word about those things.

Diane Mulligan:

I think advocacy is also so important because when people see you, you don't look like a lung cancer patient. I'm not sure what a lung cancer patient looks like anymore, to be perfectly honest with you, but you certainly don't look like one. You're healthy, you're vibrant, but yet you're still dealing with lung cancer. So what do you want people to understand who haven't gone through the journey down the road that you're on right now?

Stephanie Williams:

Well, something we often say in LCFA is that anyone with lungs can get lung cancer. And I think that's my biggest message when I do meet someone who might say, "You don't look like you have lung cancer," or just be shocked to learn that I do. Yes, even young people can get lung cancer. Yes, even non-smokers can get lung cancer. And having those conversations, I think is the best way to start to bring down the stigma that surrounded lung cancer for so long.

Mitch Jelniker:

We talked about your advocacy in helping others facing lung cancer, but it's also important for lung cancer patients to advocate for themselves, isn't it?

Stephanie Williams:

Yes, absolutely. And that comes back to knowing what questions to ask. And something that helps with that are podcasts like this one, resources like LCFA, and fellow patients support groups, anyone who has been in the game a little bit longer than you usually has some wisdom to share. And I find that really helpful.

Diane Mulligan:

Well, you're a great advocate and you really do help people a tremendous amount. Is there anything else you want to tell them?

Stephanie Williams:

I'm happy to be here, Mitch and Diane, and the reason I am here is because of the research that's already been done, clinical trials that have already been ran. And if we could keep this research going, I know myself and the other patient advocates plan on being here a very long time to help that cause moving forward.

Diane Mulligan:

We really look forward to continuing to work with you. It's really an honor. Thanks so much.

Stephanie Williams:

Thank you. It was great being here with you both.

Mitch Jelniker:

Thank you.

Diane Mulligan:

What struck me the most about these conversations about STK11 was the importance of knowing your biomarker. As Dr. Punekar put it, STK11 is the new kid on the block of biomarkers.

Mitch Jelniker:

And for Stephanie, knowing her biomarker allowed for more targeted therapy options, and doctors can offer more specific treatment paths thanks to what is learned from clinical trials. So if you're enjoying this Hope with Answers Living with Lung Cancer Podcast, consider donating to help LCFA produce this resource. And remember, this podcast is a resource for patients or really anyone else seeking answers, seeking hope, and access to updated treatment information, scientific investigation, and information about clinical trials.

Diane Mulligan:

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