Transcript - How Immunotherapy Is Changing Lung Cancer Treatment

Diane Mulligan (00:00):

Imagine if your immune system could be trained to hunt down and destroy cancer, kind of like a bodyguard who's fighting for your survival. That's the power of immunotherapy. Hi, I'm Diane Mulligan.

Mitch Jelniker (00:14):

And I'm Mitch Jelniker. So instead of attacking cancer with outside forces like chemotherapy or radiation immunotherapy kind of supercharges your body's natural defenses, teaching them to recognize and then eliminate cancer cells.

Diane Mulligan (00:29):

And for lung cancer patients, this breakthrough means longer survival fewer side effects, and new hope where options were once very limited.

Mitch Jelniker (00:41):

So let's meet someone who's been on those front lines of immunotherapy research, a Lung Cancer Foundation of America grant recipient who has dedicated her life to exploring immunotherapy.

Diane Mulligan (00:52):

Dr. Kelly Smith is the associate professor of oncology at the Bloomberg Kimmel Institute for Cancer Immunotherapy at Johns Hopkins Medicine. Dr. Smith, we are so excited that you're joining us today. Thank you so much. Can you, you know, let's just jump right in and I wanna know more about your lab. I'm so excited to hear about it.

Dr. Kellie Smith (01:13):

Yes. Thank you both so much for having me. Um, so my lab is primarily focused on researching lung cancer and particularly in the early stage setting. So traditionally immunotherapy was approved in advanced metastatic disease, and now it is approved in resectable lung cancers. And my lab is really focused on understanding how, uh, immunotherapy works in this early stage setting and what are the correlates of response or resistance and long-term clinical outcomes in patients who are receiving these therapies.

Mitch Jelniker (01:49):

You know, scientists began uncovering how the immune system kind of interacts with cancer, maybe as far back as the fifties, 1960s. But in terms of modern medicine, when was that kinda aha moment when we discovered our own immune system may help us battle cancer?

Dr. Kellie Smith (02:05):

We often say in science, there are no eureka moments. There's moments, uh, there, you know, there's things that kind of don't quite make sense. And, uh, the interface between the immune system and the cancer is, is no different. Uh, so really it's been a decades long discovery, um, trying to get to this point where immunotherapy has really transformed the lives of, of cancer patients. But really, all of this started

with this very first clinical trial that was published in 2010, um, where they were looking at blockade of this molecule called PD one that they had shown in mouse models could dampen t-cell responses. So if you block this, the theory was maybe we can enhance the immune system's response to cancer. And there were a few response clinical responses in this initial clinical trial, and some of them were in lung cancers. So, uh, they took this, you know, very preliminary first in human phase one trial. They saw that this worked in a few patients who had lung cancer and then just, just ran with that, uh, right out of the gate and started doing these trials in lung cancer and saw that you had this very nice 25% response rate in, in patients with lung cancer.

Diane Mulligan (03:24):

I just love that where you said there. Moments. That's, that's so interesting. And, you know, I think it helps us when we are looking at how much time has to go into a, a big change like this. How has the advent of immunotherapy really changed the treatment landscape for patients?

Dr. Kellie Smith (03:43):

It's absolutely changed, uh, completely even in the amount of time that I have been, uh, working in this field. Um, so what we're seeing is there are patients who now don't even see chemotherapy. Uh, it is a small percentage, um, because a lot of our immunotherapies are in combination with chemotherapy, but a lot of patients are receiving this now in the first line. So they're not getting just your standard run of the mill chemotherapy anymore. A lot of times it's either immunotherapy alone or immunotherapy in combination with chemotherapy. Um, so this has really resulted in a complete shift in, in how we're treating patients, a shift in how we're measuring clinical outcomes and clinical responses, and then also how we're managing side effects, which, um, seem to be a lot less in, in immunotherapy relative to chemotherapy.

Mitch Jelniker (04:37):

That's, that's encouraging. It really is. And, and I gather this isn't like so many things with lung cancer, one size fits all. So what would you say are the main types of immunotherapies used for lung cancer and how do they work exactly?

Dr. Kellie Smith (04:49):

The primary immunotherapy currently being used is blockade of the PD one or PD L one pathway. Um, there are also other immunotherapies that are approved targeting other molecules like CTLA four and LAG three. Those aren't used in lung cancer, uh, terribly frequently. Uh, really it's primarily blockade of, of PD one and PD L one. And what these are, are, uh, antibodies that are synthesized by the pharmaceutical company and they essentially block the ability of the, uh, tumor cell to shut down T cells. Um, so this is a mechanism that tumor cells have evolved to kind of grow and evade our immune system. And what we are able to do with these drugs is go in and block this so our T cells can really go in and do what they're supposed to do, which is kill malignant cancer cells.

Diane Mulligan (05:43):

Dr. Smith, what determines if a patient is a really good candidate for immunotherapy

Dr. Kellie Smith (05:49):

In general? Uh, the, the patients who are are most likely to respond well to an immunotherapy, um, will have tumors that do not have mutation mutations in the EGFR pathway, uh, ROS one or alk. Um, these are tumor types that in general do not respond very well to immunotherapy. Um, and, and really it tends to be, uh, lung cancers that are associated with, uh, a history of smoking. Um, those more often will respond better to immunotherapy or those with a high number of mutations, which is something that your doctor will test for if and when you are diagnosed with lung cancer.

Mitch Jelniker (06:33):

Very good. Are there specific biomarkers that can predict a patient's response to immunotherapy?

Dr. Kellie Smith (06:39):

There are some that are used. Uh, but, but truth be told, they aren't terribly good at doing what they're supposed to do. Um, there is a molecule called PD L one, which is expressed by the cancer cells that in some studies has been shown to, uh, to be higher in tumors that will respond better to immunotherapy. But this is a highly imperfect biomarker. Uh, also the high number of mutations, which I mentioned a few moments ago, again, in some studies, has been shown to be predictive of response. Um, but really in the real world, uh, uncontrolled setting, um, not like a clinical trial, you know, in real world with real patients, this really hasn't borne out to be a very effective way, uh, of predicting. So outside of the, um, the mutations like EGFR, ALK Ross, those things, we know in general, those tumors are not going to respond outside of that, there aren't really very good biomarkers.

Diane Mulligan (07:41):

Interesting. You know, I'm always fascinated to talk to somebody like you because this is my favorite question. What are the advancements that are going on right now in lung cancer immunotherapy? Where are we going? What excites you?

Dr. Kellie Smith (07:55):

It is a really exciting time, um, because just again, in, in the short amount of time that I've been in the, the lung cancer research community, um, really it has exploded into all of these different avenues that we're now discovering. And, uh, you know, up until 15 years ago, we didn't view lung cancer as an immunogenic tumor because the survival was so poor. Um, but what we're seeing is that it actually can be very immunogenic and we just need to better understand how we can harness the immune system to overcome all of these negative things that the tumor is doing to it. Um, so what I am most excited about now is this avenue into more precision immunotherapy approaches. So if we can learn about specific types of tumors, we can then tailor patient treatments to the, the tumor that they have. Um, so these will be things like, um, specific types of T-cell engagers, which is a new of immunotherapy that I personally am very excited about. Um, perhaps adoptive cell therapy or CAR T cells, um, are also things that I'm excited about. And then also targeting other molecules besides PD one. So PD one is the most well studied checkpoint, um, molecules. So, uh, but, but there are other ones that are out there that are very exciting, um, and that I think hold promise in the near future.

Mitch Jelniker (09:22):

You, you mentioned earlier that some patients may not, uh, need chemotherapy. And so, and some, some might. Does that mean that perhaps immunotherapy is better tolerated than chemotherapy?

Dr. Kellie Smith (09:34):

Absolutely. Uh, so immunotherapy is, is much better tolerated, uh, than traditional chemotherapy. And, and even the chemotherapy, uh, that we give patients today is not, you know, your grandmother's chemotherapy. Um, so the, you know, a lot of times what I, what I hear from people is, I, I'm not going through chemo again. You know, I did it 30 years ago, I'm not doing it again. Um, but what I always try to tell folks is the chemotherapies are a lot different nowadays. Um, they, they are better tolerated. They're still not fun by any stretch of the imagination. Um, but we also have better ways of, uh, managing side effects and mitigating, uh, the very adverse effects of chemotherapy. But in general, immunotherapy is much better tolerated. And my personal goal would be for no one to ever have to go through chemotherapy. Um, so that is something that as an immunologist, if we can develop better me better methods of activating the immune system without putting patients through chemo, that would be amazing. From my perspective.

Diane Mulligan (10:36):

I think that is so important. I'm interested if you go all the way back to the beginning, how important was this LCFA early career s researcher grant to you in getting into studying immunotherapy, immunotherapy and lung cancer and, and pushing? You know, we, you've really been on the forefront of pushing forward our knowledge about the, how the immune system works. How important was it to get those seed, that seed money to get started?

Dr. Kellie Smith (11:04):

It was, it was crucial. Um, so, so the grant that I received from LCFA was the first grant I ever received, um, as, as an independent investigator. Um, I think at the time, I, I had just started my, um, faculty appointment, um, and it was the first grant that I, that I ever got. And it allowed me to do those preliminary studies that, um, I used as data in my larger grant applications to the, like the NIH and the DOD. Um, and it was also fundamental in, in developing some of these studies and generating some of the data that accompanied our clinical trial report in, in the resectable lung cancer setting. Um, this was the very first clinical trial of immunotherapy in early stage lung cancers. And this was published in the New England Journal in 2018. And the funding from you guys allowed me to do some of those correlative studies that really supported furthering this treatment approach in the phase three study that was then published a few years later. So, um, not only was it good for me personally, but, but I think in the, in the global scheme of things, it was great for, for advancing this therapy into an FDA approval.

Mitch Jelniker (12:24):

That's awesome. And, and you were nominated and received a merit award, which provides a, I believe it's additional couple years of funding, explain the significance of a merit award?

Dr. Kellie Smith (12:34):

Yes. Uh, a merit award is a mechanism through the NIH where early stage investigators who are receiving their first RO one, um, if they receive a high enough score on their grant, they are eligible to receive instead of the five years of funding, they're eligible to receive two additional years after their five years is, is completed. So, um, I was, was lucky enough using the data that was generated from my LCFA grant, um, to receive one of these awards. My grant was, was reviewed very highly and very favorably. So I was able to get seven years of funding instead of five. That's awesome

Diane Mulligan (13:15):

That those years of funding are so important. You've been doing this work, not only has this advanced work in lung cancer, but your work is also advanced work in other types of cancers, which I think is amazing and I know how dedicated you are. How do you make that work life balance? You're a mom, you've got, you know, you've got everything going on at home, you have your own lab. What advice do you have for other women who might be going into the field and how they can really navigate this whole area?

Dr. Kellie Smith (13:46):

That's an excellent question, and one thing that I am very, uh, fortunate to have is a team of excellent people who work with me. Um, my lab is wonderful, um, and I really, you know, when I'm done at the end of the day, I am able to go home and my lab is able to go home, and we're able to enjoy our time with our families and enjoy our time off. And then when we come back to work in the morning, we're ready to work and we're ready to be dedicated. Um, so I, I think number one, having an excellent team of people is very important, um, and, and making sure your team is happy, um, and they really enjoy the work that they're doing. But also, you know, you asked about work-life balance. There has to be a work-life balance mm-hmm <affirmative>. Um, because unhappy people don't do well in their jobs. Um, and this is something we constantly need to remember for ourselves, but also for the people who work with us. Um, so I, I very much take pride in, in making sure, um, my lab is, is happy, my lab has a work-life balance, but then also that I'm able to kind of clock out at the end of the day.

Diane Mulligan (14:59):

That's great. I think that's so important. I, I can't tell you how much we appreciate you taking the time today to chat with us. It's been, uh, it's been eyeopening and it's also so hopeful. Yes. I mean, when you think back, this started back in 2010 and where we are today, and then when we talked to you about where we think it's going and that specialized medicine, that precision medicine, it just, um, it just brings a smile to your face that we're making advances, especially in a disease that was considered just a death sentence not that long ago.

Dr. Kellie Smith (15:30):

It really is, um, an an exciting time for the research community and, uh, you know, nothing would make me happier again, you know, if no one had lung cancer, that would be wonderful. Um, but, but second to that, I think nothing would make me happier than if we can turn this into a manageable disease.

Mitch Jelniker (15:50):

Absolutely. Excellent. Dr. Smith, thank you. We appreciate your time. Thank you so much. Uh, Diane, you, you hit the nail on the head there. Uh, talking about hopefulness, we talk about research going on every day. There is someone who is on the front lines, and you can hear the positive hopefulness in her voice of the, the, the, the advances they're making. Um, each month, each year. It's, it's great to see

Diane Mulligan (16:13):

What an exciting area of research for her to be in. And I really hope that people think about this area of research because it is so exciting and there have been so many breakthroughs and think of the impact that she's had, not only with lung cancer patients, but with cancer patients around the world. It's just phenomenal.

Mitch Jelniker (16:31):

So if you'd like to find more information about the, the latest of lung cancer research, the new treatments, and so much more, just go online@lcamerica.org. And you can also join the conversation with LCFA on Facebook, on Twitter, and on Instagram.