



PD-L1 Testing for Lung Cancer: How Your Score Determines Treatment

Dr. Julie Brahmer (00:00):

We are very excited about all the treatments that we have now to treat cancer, get the cancer under control, and for some patients to cure their cancer, but we can always improve things.

Intro Voiceover (00:13):

Living with lung cancer looks different for everyone, but no one should go through it without answers. This is Hope with Answers, where patients lead and experts help guide the way.

Colette Smith (00:24):

Hi, I'm Colette Smith and I'm living with lung cancer. Today we are going to explore PD-L1, what it means, what it may mean to patients. I'm here with the subject matter expert, Dr. Bramer from John Hopkins University Hospital. Good morning, Dr. Ramer.

Dr. Julie Brahmer (00:45):

Good morning. I'm certainly happy to be here to be able to explain some of my research and my interest in lung cancer to be able to help explain some of the things.

Colette Smith (00:58):

Okay. Thank you for your presence here and thank you for all that you do. I hear the term PD-L1 a lot and I really want to understand what it means to patients living with lung cancer and how it may impact treatment.

Dr. Julie Brahmer (01:14):

So PD-L1 is otherwise known as program death ligand one. And what that is is a protein that's expressed on a cancer cell or other cells in your body to help control the immune response or your white blood cells response to them. And that is important because that protein will connect to something called PD-1 or program death one, which binds PD-L1 from a white blood cell to your cancer cell and then that shuts down the white blood cell and prevents the white blood cell from attacking the cancer. And so we think it's one pathway called a checkpoint pathway that helps your cancer cells evade or not be recognized by your immune system.

Colette Smith (02:11):

So when someone is diagnosed with lung cancer, when does PD-L1 testing come into play? When is that important?

Dr. Julie Brahmer (02:20):

So for most folks with non-small cell lung cancer, the PD-L1 level is important to know regardless of the stage. And we use that upfront to decide what treatment you should receive first. Now, you also need to know besides PD-L1 also the mutations that your cancer has because sometimes there's certain situations where the mutations help us decide what drug to give first. And so when we're talking with a patient, particularly those patients with metastatic lung cancer where we really need a drug or drugs to control the cancer quickly, all that information is used to decide which treatments we should start with.

Colette Smith (03:14):

You mentioned levels. Can you explain some more for us about levels? What does that mean?

Dr. Julie Brahmer (03:21):

So when a pathologist looks at the biopsy specimen that was used to diagnose your lung cancer, they look underneath the microscope and they also stain the PD-L1 protein. When they look underneath the microscope, they see how many cells are expressing or staining for PD-1 or PD-L1. And if it's all of the cells, or we call it 100%, that's a score of 100. If it's none of the cells, that is zero. And there's levels all the way in between because what we call it, it's a continuous variable from zero to 100%. The higher the level that it is, the more likely immunotherapy by itself will work for your cancer. But even patients with PD-L10 can also respond to immunotherapy or their cancers can be controlled by immunotherapy, even if it's zero because remember the biopsy is just one snapshot of the cancer in your body and levels can vary, but for patients with PD-L10 or no staining on that biopsy specimen, immunotherapy by itself is not very likely to work compared to if the pathologist sees all of the cancer cells or a hundred percent of the cancer cells in that biopsy specimen express the PD-L1.

Colette Smith (05:08):

So depending on my PD-L1 level, what are some of the questions that you suggest I would ask my oncologist to determine a treatment option, whether it would be treatment with immunotherapy or a combination of immunotherapy and chemotherapy? What do you suggest?

Dr. Julie Brahmer (05:28):

Yes. So one, you need to know what the level is. So depending on the number, if you have what we call PD-L1 high lung cancer, that means that 50% or greater of the cancer cells are expressing PD-L1. Then single-agent immunotherapy drugs can be used by themselves to control the cancer. Now you can also add chemotherapy in those situations and increase the chance of the cancer shrinking compared to just the immunotherapy by itself. But there are some patients with not a lot of disease and hardly any symptoms where immunotherapy by itself may be the right choice, but there are other folks, even with those levels, if they're very symptomatic or have a lot of cancer that we can see on scans, then we may elect to do combination chemotherapy with immunotherapy, but the starting point is what is the level? Now, patients whose cancers have PD-L1 low or zero, we typically recommend doing chemotherapy plus immunotherapy together because that's the best chance to try to get the cancer under control because immunotherapy by itself may not work as well.

(06:59):

Does that make sense?

Colette Smith (07:01):

Makes sense. Makes sense. I was diagnosed 11 years ago and biomarker testing wasn't quite popular then. And at the time of diagnosis, my biomarker was EGFR insertion exon 20, I believe it was. Is it a good thing? Now I'm living with an upper left lobectomy and however, I have several nodules on my right lung. Is it a good thing to have a conversation with my oncologist about possible biomarker testing for PD-L1? How may that benefit me? And to add to that, is it possible that my specimens are still up to the task for proper biomarker testing 11 years ago from 11 years ago?

Dr. Julie Brahmer (07:53):

So for patients who have been diagnosed a very long time ago and now they're needing treatment again or things are changing and the cancer is growing, we typically recommend getting a new biopsy. We can go back to the old, but that long ago things can change in your body. The PDL1 levels can change, but also depending on the treatment that you've had so far, other things like MET or HER2, those are different proteins can also change. And so I personally would recommend getting a new biopsy for you if the cancer is changing and we need to decide on new therapies. In someone who was diagnosed maybe a year ago and started on treatment for PD-L1, we typically would not repeat another test because it's been not so long and we're looking at what to do after immunotherapy. But for those patients, say a new test came along like HER2, which in the past we didn't look at for lung cancer, but now for patients with adenocarcinoma of the lung, that's a subtype of non-small cell lung cancer, we will do a new biopsy and check for that.

(09:26):

Also, another protein that we look at on the cell called MET, we can also stain and so we might repeat that. So every time that you're thinking about changing treatment, you need to ask your physician, "Is it worth repeating a biopsy?" Back in the day, maybe even five years ago, we never did that. We never asked about doing a new biopsy very often, but now in 2026, we are repeating biopsies and folks based on what treatments we have coming or potentially even what clinical trials might be going on and how we can decide what treatment to do next.

Colette Smith (10:17):

Okay. It sounds from what you're explaining that there are current research processes that are possibly going on that may even heighten treatment options for patients who are considering immunotherapy. What do we have to look forward to as lung cancer patients with regards to this research?

Dr. Julie Brahmer (10:42):

So for immunotherapy research for non-small cell lung cancer, we're looking at how to personalize immunotherapy better and PD-L1 levels are just one way, but folks are looking at other ways about how best to personalize immunotherapy. Also, we're trying to figure out how best to make immunotherapy work, what combinations of immunotherapy, new combinations of combining what we call targeted therapy with immunotherapy or other types of immunotherapy or immune type treatments like how to re-engineer somebody's T-cells. Those are called CAR T-cells or also using things called vaccines where we're trying to train your immune system to respond to a protein that might be expressed on your cancer cell.

Colette Smith (11:49):

Vaccines, that sounds promising, especially as it pertains to lung cancer and the possibility of avoiding invasive treatment. Is there ever a time where immunotherapy can adversely impact a patient during treatment?

Dr. Julie Brahmer (12:11):

Yes. Unfortunately, these treatments all have side effects. Typically, they're not the same as chemotherapy or even the same as targeted therapy, but when we're trying to take the brakes off your immune system or allow your immune system to recognize the cancer, your immune system can go into overdrive or actually recognize normal cells and try to attack them. So immune therapy can affect your normal cells and that causes side effects and that's by releasing your immune system and your own immune system is attacking your normal cells. Now, bad side effects where we have to stop the immunotherapy and give medications that actually reign back the immune system occurs maybe one out of 10 times in patients. So it's not very often, but certainly when it does, it can have even short-term effects, side effects, as well as potentially long-term side effects. So those are kind of the drawbacks.

(13:24):

Now, more common side effects are effects on the thyroid. So some people, their thyroid no longer works and so we have to give them thyroid hormone. Other times, another common side effect is a rash. Typically, we can treat that by topical steroids to try to control that rash. Sometimes it can just be itching, so there are medicines to control the itching. And then there's other side effects like diarrhea, which is if your immune system attacks your bowels. And so for some patients there, we have to start a medication called prednisone or what we call steroids to arraign back the immune system. But typically, again, like I said, bad side effects where we have to stop the immune therapy, put people on high doses of steroids. That doesn't occur very often, but when it does, it gives us pause. We have to place people on these steroids, slowly taper them off.

(14:26):

Depending on the side effect, we may or may not feel comfortable restarting the immunotherapy, but the beauty of these type of treatments, even if something like that happens and we don't feel comfortable restarting the immune therapy, for folks where the immunotherapy is working and we have to stop the drug, your immune system can still continue to work even though we can't give you another dose. And so for some folks, it continues to work for a very long time and you just don't need another dose because it's also not safe. For other folks, we have to pivot and use a different type of treatment, but really it depends on what's going on at that time. But you're right, there's no drug that we don't have or that we have that would not have a side effect and these just have different side effects. And unfortunately, some of the side effects are long-lasting.

(15:28):

So if someone needs thyroid hormone because their thyroid no longer works because of something I gave them like immunotherapy, more than likely you have to stay on that thyroid hormone forever.

Colette Smith (15:43):

We've discussed a lot today. We've used a lot of acronyms, PD-L1, EGFR, exon 20. We've spoken about immunotherapy. And what I'd like to know, because I'm sure there are many, many survivors out there who are relying on this information to possibly have conversations with their physicians, what would be

some takeaways that you would advise lung cancer patients of questions to ask their physicians when seeking treatment options?

Dr. Julie Brahmer (16:20):

So those questions will depend on where you are on your treatment continuum, but if you're first diagnosed and you've just been diagnosed with lung cancer, particularly non-small cell lung cancer, you need to know several things and ask, have these tests been done on my cancer? One would be one, has the staging been completely completed? So do we know, do I have cancer in my brain? Where is the cancer at this point? So that's called staging.

(16:54):

Next is for the biopsy that was taken, what testing has been done? For non-small cell lung cancer, typically that is mutation testing. So they look at the genes of the cancer. Are the genes abnormal or what we call mutated or fused differently? So that's a fusion or a mutation. And then also what is your cancer's PD-L1 score? So how much PD-L1 does your cancer express? And depending on those, all those results will help your oncologist decide what type of treatment should you receive either before or after surgery, if you have early stage lung cancer, after chemotherapy and radiation in what we call locally advanced lung cancer, or in metastatic lung cancer, it also helps us decide what type of what we call systemic treatment, either targeted treatment, chemotherapy, and/or immunotherapy should be used.

Colette Smith (18:03):

Dr. Bramer, I am a part of an affinity group of about 30 women that look like me who are all lung cancer survivors and there are several women in this group who have benefited from clinical trials and others who have not. There's one person in particular, I won't mention names, and it just breaks my heart that she has not been able to benefit from any of this wonderful medicine. In addition to PDL biomarker testing, are there other things that she may do to seek treatment options?

Dr. Julie Brahmer (18:42):

That's one question patients should always ask is really, is there a clinical trial that's right for me? Some people are nervous to ask about that, particularly when they're just initially diagnosed, but for some patients' clinical trials, even upfront where they've never been treated before, there are clinical trials for patients who are just starting out. And so it's important to ask every time you need to decide on treatment, is a clinical trial right for me and do you have a clinical trial available here for me or can you help me look for a clinical trial that might be right or be practical for me to be a part of? So I do think that's a very important question. We are very excited about all the treatments that we have now to treat cancer, get the cancer under control and for some patients to cure their cancer, but we can always improve things.

(19:47):

And so that's what clinical trials are for is how can we improve therapies or how can we better understand how or why or if they might work for patients.

Colette Smith (20:02):

So parallel to that clinical trials question, tell me about patients or situations where the PD-L1 immunotherapy treatment option may not work for some patients where that may not be their best option. Tell me a little bit about that.

Dr. Julie Brahmer (20:19):

Yes. So for patients who are initially diagnosed, there are particular situations where we're worried that immunotherapy may not be the best type of treatment and that comes down to multiple factors. So for patients with mutations where we have a very good targeted treatment, where the targeted treatment would work much better than immunotherapy, we would typically offer that targeted therapy because immunotherapy may not work. So that's one situation. Other situations are for patients who have organ transplants. We do have patients who develop lung cancer after an organ transplant, like heart, lung, liver, or even kidney transplant patients. In those situations, immunotherapy, if we give it, may cause organ rejection and we obviously don't want that. And so in those situations we may not want to give immunotherapy and it's a very long discussion and a nuanced discussion if we even consider it. There are other patients with known autoimmune diseases and what does that mean?

(21:36):

So diseases that are caused by your immune system. So patients with colitis, you can have Crohn's disease or ulcerative colitis that's an autoimmune disease of your GI tract, or some patients with say rheumatoid arthritis is another autoimmune disease where your immune system attacks your joints. Those patients with those types of autoimmune diseases, we sit down and talk about what type of treatment you're on to control your immune system attacking those organs and whether or not it makes sense to give you immune therapy. I would say for the most part, it's not an absolute what we call contraindication, but we are not sure how well immunotherapy might work for the cancer when we have to keep your immune system under control so it doesn't affect your normal cells.

Colette Smith (22:34):

We've spoken about a lot today. We've spoken about PD-L1 as it pertains to immunotherapy with the treatment of lung cancer. We've spoken about clinical trials, autoimmune diseases as they pertain to treatment options for PD-L1 and immunotherapy. And we've spoken a lot about science and what I hear from all of this is hope. Hope and new treatment options that are on the horizon for lung cancer patients. If you'd like to learn more about this, you can go to lcfamerica.org.