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Special Considerations in NSCLC: Treating PD-L1 High Patients

Announcer:
You're listening to *Closing the Gaps in NSCLC*, sponsored by Lilly.

Dr. Nacinovich:
Non-small cell lung cancer accounts for 80% of lung cancer diagnoses, and despite a broadening portfolio of treatments available to patients, the need for finding more targeted therapies for this disease is absolutely critical. One such development that's got more personalized approaches to treatment is the emerging biomarker PD-L1. On today's program we'll dive into current understandings of this biomarker and some special considerations for patients with high PD-L1 expression.

Welcome to *Closing the Gaps in Non-Small Cell Lung Cancer* on ReachMD. I'm Mario Nacinovich, and here to share insights with us on therapeutic approaches for patients with high PD-L1 expression is Dr. Michael Shafique, Assistant Professor of Thoracic Oncology at the Moffitt Cancer Center in Tampa, Florida.

Dr. Shafique, welcome to the program.

Dr. Shafique:
Hi, thanks for having me.

Dr. Nacinovich:
So, Dr. Shafique, to start us off, can you give us some background on the role of PD-L1 in non-small cell lung cancer?

Dr. Shafique:
Absolutely. So PD-L1 stands for programmed death ligand protein, and it has a function in normal inflammatory responses in a human body. It helps blunt adaptive immunity and helps prevent autoimmune disease. Unfortunately, this pathway is co-opted by cancers, and what it can do is the PD-L1 protein on tumor cells and other antigen-presenting cells in a patient's body will reduce the immune system's ability to fight cancer cells.

Dr. Nacinovich:
And what would be characterized as a high PD-L1-expressing patient?

Dr. Shafique:
Yes, so by most measurements, at least in non-small cell lung cancer, we assess the percentage of tumor cells that express the PD-L1 protein on their surface. We use cutoffs of 50% or greater to indicate high PD-L1 expression, and about 30% of non-small cell lung cancer patients will fall into this category.

Dr. Nacinovich:
What has the response been like from the oncology community toward adding this and other emerging biomarkers into their scope of practice?

Dr. Shafique:
So the response, at least in the community, has been very rapid in their uptake of the PD-L1 marker in their testing. It's a pretty simple test to do. It utilizes immunohistochemistry, so it's a very common procedure that pathology labs can do. It also requires a small amount of viable tissue in order to run that test, so the uptake has been pretty rapid in the community.

Dr. Nacinovich:

Have there been any hurdles to work through in terms of reliably identifying patients with high PD-L1 expression or making this testing accessible in both academic and community settings?

Dr. Shafique:
Even though it does require a small amount of tissue to run the test, I do think initially when patients would get testing of pleural effusions to test for malignant effusions or if they had bronchoscopic examinations with lymph node biopsies, we sometimes even in those small samples lacked enough tissue to run a PD-L1 test for patients, but I think most folks in the community these days are getting adequate tissue even from these samples or taking extra passes on bronchoscopic biopsies in order to have enough tissue to run these tests.

Dr. Nacinovich:
For those just tuning in, you're listening to *Closing the Gaps in Non-Small Cell Lung Cancer* on ReachMD. I'm Mario Nacinovich, and joining me today is Dr. Michael Shafique, Assistant Professor of Thoracic Oncology at the Moffitt Cancer Center.

So, Dr. Shafique, now that we have a better understanding of this biomarker and identifying high PD-L1 expressing patients, let's shift over to its impacts on your treatment approach. First, what are the specific considerations we should be factoring into the equation when selecting initial therapies?

Dr. Shafique:
Yes, in non-small cell lung cancer patients, I think the important first considerations are to look at the histology of the patient to understand if it's a primary squamous cell carcinoma or if it's a mixed adenocarcinoma or a pure adenocarcinoma sample. The second thing then to look at is additional molecular testing, and this is most important in the adenocarcinoma patients, so we would want to make sure that they have had full molecular profiling of the EGFR, of any EGFR mutation, any ALK rearrangement or ROS1 rearrangement, and then we want to look at if the patient is significantly symptomatic from their underlying disease. And so, even if a patient has a high PD-L1 expression of 50% or greater, some of these other considerations may tilt us in favor of using a different approach than the typical recommendations would be for a high PD-L1 expressor.

Dr. Nacinovich:
And once the initial treatment approach is selected, how and when do you follow your patients to confirm that the targeted therapy is working effectively?

Dr. Shafique:
So the typical guideline now is for patients who have a high PD-L1 expression, and if they are adenocarcinoma patients and don't have an EGFR, ALK or ROS1 abnormality, they start checkpoint inhibitor therapy typically with pembrolizumab, and they receive this infusion every 3 weeks, and typically after 2–3 cycles I'll repeat CT scans to reassess the treatment response. We're also following symptoms of the patients as well. Typically, if patients are responding rapidly to treatment, we'll notice significant improvement in their presenting symptoms. Other things to look out for are any rapid deterioration in their symptoms. That would be an indication that potentially their tumor is not responding as we had hoped to PD-L1-directed monotherapy.

Dr. Nacinovich:
What are some of the factors you've seen in practice that have either helped or harmed the effectiveness of PD-L1-targeted therapies in high-expression patients?

Dr. Shafique:
So we occasionally will run into patients who have autoimmune disease, and that presents a challenge for PD-1/PD-L1-directed therapy. Typically, as I mentioned previously, the PD-1/PD-L1 interaction is important to prevent autoimmune disease, so blockade of this interaction with a medicine like pembrolizumab or any of the other checkpoint inhibitors does have the risk of causing worsening of underlying autoimmune conditions. It's not an absolute contraindication to the use of these therapies in patients with autoimmune disease, but we really try to pick patients who perhaps they have rheumatoid arthritis that's been in remission for several years or they have a history of another autoimmune condition that doesn't require intensive immunosuppression. These are kinds of patients that would potentially benefit from a trial of immunotherapy. Even if their autoimmune disease worsens slightly, we could still control them and symptomatically control their worsening autoimmune disease during the anticancer treatment, but if they have a significant underlying autoimmune disease such as Crohn's disease or ulcerative colitis or they are very symptomatic from that, then immunotherapy with a checkpoint inhibitor could actually make that situation a lot worse, and we tend to shy away from initiating checkpoint inhibitors in patients like that.

Dr. Nacinovich:
Looking ahead, what's on the research or practice horizon in terms of improving detection and treatment capabilities with this

biomarker?

Dr. Shafique:
Yes, I think it's an open question in terms of whether patients with high expression of PD-L1 benefit from the addition of chemotherapy to the checkpoint inhibitor monotherapy. Currently, the preferred option is to use the monotherapy such as pembrolizumab. However, there is some thought that there are a subset of patients even with high expression of PD-L1 who may benefit from the addition of chemotherapy, and right now there are ongoing clinical trials sponsored by cooperative groups that are looking at the optimal sequencing of chemotherapy and immunotherapy to address that question.

Dr. Nacinovich:
And as we come to a close, Dr. Shafique, could you share any additional thoughts for those in our audience who are currently managing patients with non-small cell lung cancer?

Dr. Shafique:
Yes, I think probably the most important thing I would tell physicians taking care of patients with high-expressing PD-L1-positive non-small cell lung cancer is to really trust your judgment of the patient sitting in front of you. So, if they are pretty symptomatic or if you're at all concerned that even monotherapy may not be as beneficial, I think consideration can be given to giving patients chemotherapy plus immunotherapy combinations up front. It's definitely a potential option and within the guidelines to do so, so I would really trust your judgment as far as the symptoms of the patient and the clinical situation in which the patient is.

Dr. Nacinovich:
Those are all great things for us to keep in mind. And as that brings us to the end of today's program, I want to thank my guest, Dr. Michael Shafique, for sharing insights with us on effective therapeutic approaches for patients with high PD-L1 expression.

Dr. Shafique, it was great having you on the program.

Announcer:
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