Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/project-oncology/investigating-immunotherapy-its-role-in-nsclc/12452/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Investigating Immunotherapy & Its Role in NSCLC

Dr. Sands:

Dr. Sands:
Immunotherapy has led to some impressive results in cancer treatment, but not all cancers respond. Identifying those most likely to benefit from immunotherapy and managing the toxicities is an ongoing area of important investigation. And we're gonna discuss this in lung cancer with one of the leaders in the field.

Welcome to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands and joining me to discuss the role for immunotherapy in lung cancer treatment is Dr. Mark Awad, a Thoracic Medical Oncologist and Clinical Director of the Lowe Center for Thoracic Oncology at the Dana-Farber Cancer Institute and Assistant Professor of Medicine at Harvard Medical School. Dr. Awad, welcome to the program.

Dr. Awad:
Thank you very much. Very happy to be here. Thanks for the invitation to join you, today.

Dr. Sands:
So, Dr. Awad, we're gonna get to some general discussion about immunotherapy in a moment, but first let's start with lung cancer treatment options. There have been various regimens, including immunotherapy alone or in combination with chemo, that have been approved for the treatment of lung cancer. Can you take us through your treatment algorithm?

Dr. Awad:
Sure. And this has been a very fast-moving and exciting field and we're happy to have many treatment options to offer for our patients. And so when we meet a new patient with advanced metastatic lung cancer, which unfortunately today is still the majority of new patients that we meet with stage IV or metastatic lung cancer, we typically first break it down by histology, does the patient have squamous or non-squamous non-small cell lung cancer and from there, depending on the histology, we tend to order advanced molecular or genomic sequencing. So for most non-squamous non-small cell lung cancers, we will order next generation sequencing panel, either on a tissue biopsy or from a plasma sample to assess circulating tumor DNA, to look for an increasing number of targetable genomic alterations in genes like EGFR, ALK, ROS1, BRAF, MET, RET, and track HER2 and increasingly, more and more markers with every passing year, including KRAS G12C now. And if a patient has a targetable genomic alteration, we tend to start with targeted therapy first; typically these are oral kinase inhibitors that are well-tolerated and highly active with high response rates. But still, a majority of patients with advanced non-small cell lung cancer will lack a targetable genomic alteration within their tumor. And for those patients, we tend to test PDL1 by immunohistochemistry, and from there that helps us decide on the initial treatment plan.

And for patients with non-small cell lung cancer and high PDL1 expression, we tend to consider use of PD1 inhibitor monotherapy and for patients with low or absent PDL1 expression, we tend to combine PD1 with a platinum doublet chemotherapy. The cutoff that we tend to use now is based on several large phase 3 clinical trials, one of which is the KEYNOTE-24 study which used a PDL1 tumor proportion square cutoff of 50% or greater. And for those patients again, we tend to use pembrolizumab by itself for patients who have a low or negative PDL1 expression, we would combine pembrolizumab either with platinum pemetrexed for non-squamous or platinum taxane for squamous histology.

There are a number of other regimens that have been approved with immunotherapy alone or immunotherapy combinations, but that's the general approach for how we decide the initial treatment plan for patients with advanced non-small cell lung cancer.

Dr. Sands:

Excellent. So, although many tolerate the treatment well, there are side effects that certainly can come up related to these therapies. So can you outline some of the potential adverse events and how you'd recommend handling them?

Dr. Awad:
Right. These therapies have been very promising, and many studies showed they improved overall survival for patients and as you said, they are generally well-tolerated. But there are several unique and potentially serious or dangerous, even life-threatening adverse events that need to be monitored more carefully. And when I talk to patients prior to starting immune checkpoint inhibitors, I explain the mechanism of action and I also let them know that therapy side effects that we will be monitoring for, but that they should also be monitoring for, so they can let us know if they're not feeling well.

So we tend to see most patients with relatively minor side effects, such as maybe fatigue, some joint aches, maybe decreased appetite, some itching, but more serious immunologic adverse events are related to inflammation that happens in organs even where the cancer is not present. The vast majority of side effects are manageable and treatable with corticosteroids initially, which tends to dampen the immunologic adverse events from these therapies.

I tell our patients though some of the side effects that are treatable, but not necessarily reversible, are those that affect the endocrine organs. So for example, if there is hypothyroidism that results from use of the immune-checkpoint inhibitors, we'll need to support those patients by offering thyroid replacement hormone. So many of these side effects are manageable, but there have been some cases of fatal toxicities reported in the literature and particularly pneumonitis is one of the more feared complications of immune-checkpoint inhibitors. And we tell our patients to really let us know immediately if they're experiencing any new side effects that we can assess them and if necessary, intervene early. I think that earlier you catch these and treat them, the better.

Dr. Sands:
Excellent. Thank you. That's helpful in overviewing that. Now related to that is autoimmune disease. So in the development of these trials in many cases, those with autoimmune disease were not really included and given the potential impact on the interaction of the immune system with normal cells, of course, that is a very reasonable initial concern. Do we now have data on this? And how much have autoimmune disorders impact decision-making as far as treatment options?

Dr. Awad:
Right. These are really important questions. The clinical trials have generated a lot of data for us to learn from however as you mentioned, several important patient populations were excluded from these pivotal trials leading to approval of immune-checkpoint inhibitors, such as patients with pre-existing autoimmune disease, patients with HIV, patients with active hepatitis B or C have been excluded, patients with organ transplant, and so, after the approval of these drugs, we've been trying to learn as quickly as possible to understand how do these therapies perform in these populations that were ineligible or excluded from clinical trials? And we and others have looked to try to address this question in our retrospective fashion. So for patients who were not on clinical trials but received immune-checkpoint inhibitors with any variety of these conditions, we've looked to see how they have done and there are some biases in this type of analysis because, you know, perhaps oncologists more carefully select which patients with autoimmune disease they are willing to treat with immunotherapy as compared to others. But what we and others have looked for is, number one, when these patients receive immunotherapies, does their autoimmune disease worsen or flare up, and secondly, do they have other or are they at greater risks for other immune-related adverse events?

If patients have generally mild or well-controlled auto-immune disease or their disease is quiescent and not requiring systemic therapy, many patients are able to safely receive immune-checkpoint inhibitors and while we have seen some flares of their auto-immune disease, again if we catch these relatively early, or if we work closely with the patient's specialist, whether that's a rheumatologist or a gastroenterologist who's managing their disease, we are generally able to continue to treat with immunotherapy, or to manage carefully with some dose interruptions or dose holds and potentially use steroids for treating any adverse events.

There are some cases, however, where we've seen more severe flares of their autoimmune disease or high-grade adverse events that are unrelated to the autoimmune disease so, I'd say that when I see a patient in clinic these days with the preexisting autoimmune condition I'm somewhat cautious still if they have certain very active disease or they are requiring a number of systemic immunosuppressive therapies or regimens to keep their autoimmune disease under control. But if I don't have really any other options and we need to use immunotherapy to treat their metastatic cancer, I will certainly be in touch with the patient's care team, primary care physician, their rheumatologist or their other specialist to let them know our plan to start immunotherapy and then we in oncology and their other specialists will be monitoring the patients very, very carefully to see how best we can detect the presence of autoimmune disease flare or other potential immune-related adverse events.

Dr. Sands:

For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands and I'm speaking about immunotherapy with Dr. Mark Awad, a Thoracic Medical Oncologist and Clinical Director of the Lowe Center for Thoracic Oncology at the Dana-Farber Cancer Institute and Assistant Professor of Medicine at Harvard Medical School.

Now, Dr. Awad, you just highlighted some of the important things to consider around those with an autoimmune disease, but another important area for consideration as far as trial enrollment was active infections. And in many cases, those with HIV have not been included, and of course, this is a bigger area of discussion, but specifically around immunotherapy, can you outline any data related to active infections such as HIV or hepatitis C?

Dr. Awad:
This is also a really important topic because we know that patients with HIV are at greater risk for certain malignancies; there are also higher rates of tobacco use among people living with HIV and so lung cancer and other cancers continue to be a problem for populations like this. And the initial immune-checkpoint inhibitor clinical trials excluded patients with HIV regardless of whether their HIV was well-controlled or managed with anti-retroviral therapies and the rationale at that time was that we don't know whether there could be some immunologic dysfunction in these patients and that perhaps immune therapies would not work as well in these pivotal phase 3 clinical trials. And so those patients were excluded.

Now that these drugs are approved, again we've been using them in a broader patient population including patients living with HIV and we've reported on this and others, as well, that patients living with HIV can do very well with immune-checkpoint inhibitors. They tolerate that therapy well, similarly to individuals that do not have HIV. You can safely prescribe anti-retroviral therapies concurrently. We don't necessarily see any higher risks of immune reconstitution symptoms or issues when anti-viral therapies are started around the same time as immunotherapy, and we can still see bona-fide and durable responses to immune-checkpoint inhibitors among patients living with HIV.

We're also learning more about patients with hepatitis C and have hepatitis B and particularly from the hepatocellular carcinoma literature where we know that viral hepatitis can be a risk factor for HCC, or hepato-cellular carcinoma, and again in many cases, the new checkpoint-inhibitors can be administered quite safely and effectively in patients with these active viral infections. Of course, now we've got really terrific therapies to treat viral hepatitis and so when we have patients with active hep B or hep C, I tend again to work with our hepatology or infectious disease colleagues to see if we can manage those active viral infections while we're also managing their malignancy with immunotherapy. So these are big topics, requiring additional study and additional awareness, as well as advocacy because many of our patients who have these other medical conditions or comorbidities do not have access to current and modern clinical trials unfortunately.

Dr. Sands:
Well, ongoing advances in cancer treatment are obviously still needed, but it has been exciting to see some of the advances that have happened with immunotherapy. I wanna thank my guest, Dr. Awad, for providing and overview of important considerations for immunotherapy treatment. Dr. Awad, absolute pleasure to have you on the program.

Dr. Awad:
Pleasure is mine. Thank you so much for the invitation.

Dr. Sands:
I'm Dr. Jacob Sands. To access this and other episodes in our series, visit ReachMD.com/ProjectOncology, where you can Be Part of the Knowledge. Thanks for listening.