



## 2022 Case Based Panel Discussion

### Immunotherapy in Stage III NSCLC

#### Speakers:

**Dr. Ibiayi Dagogo-Jack:** Thoracic oncologist, Internal Medicine/Medical Oncology, Massachusetts General Hospital, Instructor, Medicine, Harvard Medical School

**Dr. Kathryn Arbour:** Medical Oncologist, Assistant Attending Physician, Memorial Sloan Kettering Cancer Center

#### TRANSCRIPT

Dr. Dagogo-Jack: And so let's move on to a different case. Again, our hope is to discuss a variety of different presentations and how we manage them. And so this is a bit different. So this is a 65 year old man who has an enlarging pleural effusion, but a little bit of background for him. So he has a history of hypothyroidism and hypertension. He has never had a smoking history or significant tobacco exposure. And about a year ago, before he's meeting you today, he had a stage three lung cancer that did not express Pd-I1. That was an adenocarcinoma.

And because of the extent of the disease and also his functional status, meaning how well we felt he was able to tolerate more aggressive things such as surgery, he got chemo radiation at the same time. So with weekly CarboTaxol, which is a regimen we often use and based on the stage of his cancer and the treatment approach, there was the option to potentially give a different immunotherapy for a year after called durvalumab, but we elected not to give him their durvalumab. About a year later, he's having his routine images, which we do to monitor the state of the cancer.

Then we see that he has an enlarging pleural effusion so fluid outside of the lung. It's outlined there in red. He also has one single focus that lights up on a subsequent Pet scan in the bone. And so it was it's a little bit controversial about what do we do with durvalumab in this setting. So it depending on where you live in the world. It may not actually be an option. So if you lived in Europe and you have a tumor that does not express Pd-I1, there's not an option to give durvalumab. But in the United States, we have the option of giving it irrespective of whether or not the cancer expresses that immune therapy marker Pd-I1.

So, Kathryn, what is your practice around durvalumab, recognizing that this is a forum for us to kind of discuss what we do, but your doctor may do something different.



Dr. Arbour: So I think one thing to keep in mind, with immunotherapy agents such as durvalumab, you saw another study indicate nivolumab, another drug pembrolizumab, we as medical oncologists think about these drugs, all similarly as immune checkpoint inhibitor, a class of immunotherapy, a type of immunotherapy, but we think of them fairly interchangeably, even though they may have different FDA approvals that are slightly different. And the category of therapy is pretty similar. So that's one thing I will say. And we also want to think about who benefits from these drugs.

Typically, when we look at big populations, which of the patients not absolute 100% guarantee that someone will have response or a 100% guarantee that they will not. But in general, who are the patients that most likely benefit from these treatments? In general, patients with high Pd-I1 expression, which is a marker on the cancer cell surface, are patients who are most likely to benefit from these immune checkpoint inhibitors. And those types of expressions are also found frequently in patients who have a history of smoking related malignancies.

So those are two categories of patients, you know, that we think of being more likely to respond to these medicines and having benefit. The challenge is that these medicines also have potential toxicities. And unfortunately, we could be in a situation where as a medical oncologist, where we don't want to be, which is where we recommend a treatment and administer a treatment, but that treatment does not work and leads to toxicity. So all of us are trying to balance the risks versus benefits.

And so in this situation, when a patient has two features that I would think that they would less likely respond to immune checkpoint inhibitor, that being absent Pd-I1 expression, a Pd-I1 negative tumor and no history of tobacco exposure, I would think they likely would have fairly minimal benefit from durvalumab or checkpoint inhibitor therapy. And in my practice, well, it might be something that we would discuss. We would also discuss the potential risks of therapy in this setting, and we may opt not to proceed with treatment.

And I think that right now there's not necessarily compelling evidence in this group of patients that durvalumab is helpful. One thing that I think is crucial in all of these patients that isn't required but can be very helpful is molecular testing with that next generation sequencing testing we talked about, this is a patient who may have an EGFR mutation or another actionable driver. They have minimal history of tobacco exposure and yet they have developed lung cancer. And so again, looking for those mutations even in this setting might be helpful to provide further context about would these medications be likely to work, would they be safe? What other therapies might we consider in that setting?