Case Based Panel Discussion 2019- Lung cancer Unresectable NSCLC

Case Based Discussion Panel – Stage 3 NSCLC Best Schedule – Durvalumab/Imfinzi in Varying Patients

Dr. Millie Das specializes in the treatment of thoracic malignancies. She sees and treats patients both at the Stanford Cancer Center and at the Palo Alto VA Hospital. She is Chief of Oncology at the Palo Alto VA and also leads the VA thoracic tumor board on a biweekly basis.

Dr. Matthew Gubens is a thoracic oncologist who treats patients with lung cancer, mesothelioma and other thoracic malignancies, including thymoma and thymic carcinoma, which are rare tumors of the mediastinum. He is an Assistant Clinical Professor of Medicine at UCSF.

Recently the doctors sat down to discuss a series of case-based scenarios. In this video, the doctors discuss the standard treatment of chemotherapy and radiation followed by immunotherapy and the best schedule for Durvalumab (Imfinzi) in a variety of patient scenarios.

Dr. Jack West: Let's say you have a patient who is older in their eighties, a bit fragile, but they were able to get through chemo and concurrent radiation, a weekly carboplatin pack, the Taxol. They've recovered okay. Do you have any hesitation about offering Imfanzi durvalumab immunotherapy to patients who are older and somewhat frail, but were able to get through chemo immunotherapy up to that point and don't have a signal that they should not get this?

Dr. Millie Das: No. I mean, I generally don't have a hesitation there. I mean, again, kind of if the patient's willing to come in every two weeks for their infusion and want to, you know, be aggressive, and feel that they are recovered, fully recovered after their chemo radiation, I wouldn't have an issue with giving it to them.

Dr. Matthew Gubens: Chemo Radiation is one of the toughest things we do in lung cancer clinics. So if you get through that and in good shape, honestly, the year of durvalumab is probably significantly less toxic with exceptions. But on the whole, if you get through that, that's a pretty darn good credential.

Dr. Jack West: Let's take the setting of a patient who is started on durvalumab doing okay, but the novelty begins to wear off at seven or eight months. And I feel that that year is a

challenge of attrition. Even if you don't have a prohibitive issue, the every two week treatment if they start to have concerns about this, I mean, we're in the Bay area, people may have long drives to get in. Do you feel that it would be acceptable to change the schedule to do like a month, every four weeks, now that there's some data for this or do you feel that it's most appropriate to just hue to the schedule or maybe even stop early? Just because we don't know how long we should do this and that there's nothing magical about a year. So how do you feel when a patient says, you know, it's been eight months, do I really have to come in every two weeks at this point?

Dr. Matthew Gubens: Again, it's just a data free zone and I think it's a conversation. Like you say, if it's not, there's no magic to the year. If we've gotten through eight or nine months and the patient feels very strongly just quality of life wise, I tend to think there's probably good likely that they've gotten the benefit they're going to get. I haven't done the four week scheduling, but there's so much precedent now in the stage four setting of, for example, Opdivo or nivolumab, the four week really similar to two week benefit. I don't think it's a big stretch hasn't come up. My patients are pretty motivated, but I wouldn't have a major priority problem with it, especially at month eight.

Dr. Jack West: Yeah. And I think also we just don't have data. So who's to say, Millie?

Dr. Millie Das: I mean I think I'm at the, in my VA practice, you know, if there was an FDA label for the four week, I would absolutely go over to that. But you know, we don't have that. And so I, you know, I, I can't do that. I'm not sure if private insurers would actually cover that, the four week. So just from the logistical standpoint, I'm not sure that'll work. I typically see these patients once a month and they're getting their, you know, one of their infusions sort of on their own and they're going to the infusion center without seeing me. So it kind of shortens their visit. And so it's a little bit more tolerable for them to be going through. And I too, you know, if they've gotten through eight months, they're kind of tired of it. I don't push them to make it to a year.

Dr. Jack West: Let's take the situation of a patient who has gotten through a year of durvalumab after chemo and radiation and they are nervous. They are grateful that they don't have evidence of relapse recurrence on their last scan, but they are really fearful of stopping. And the Pacific trial upon which our treatment is based, gave up to a year, but stopped at a year. If you have a patient who is a year in and says, I don't mind coming in, I really feel better on treatment. This is probably more likely at the Stanford practice then at the VA, but maybe at UCSF and certainly some of the tertiary care centers will have more patients who are seeking more care than we know is beneficial. What's your view there? Would you strongly dissuade patients from this or are you open to that? I mean presuming that you didn't have the barrier of coverage, which I think is an easy out.

Dr. Matthew Gubens: I would really strongly urge them to stop. Again, it's not a stage four setting, it's a curative setting and here's binary just takes us five years or so to figure it out if it happened. I would actually push them pretty strongly to say we've got a huge of this trial. There's rationale to say that a year is sufficient. There's not data for longer in this setting and really strong leaders. And I also remind them that even if the first year went well, there are unlike chemo, which tends to kind of accrue more side effects as you get deeper in, cycle six is always harder than cycle one, immunotherapy side effects can happen on day one. They can happen on day seven, 22 and so you really, very idiosyncratic. So I kind of remind them of that and say I've had enough patients in my practice where if I'm giving drug that I'm not sure it's helping, but I can sure effect your thyroid. I can sure affect, like I said, my patient with a pancreas that, you know, with new autoimmune diabetes, these things that affect quality of life also. So I would push pretty strongly to stop after.

Dr. Jack West: Now obviously the VA is going to just double over laughing, You want to do what? But I mean if you were covering at Stanford, at the cancer center at Stanford that day, you had a patient, what would your, what would your guidance be if you weren't limited by payer concerns?

Dr. Millie Das: Yeah, I think my sentiments aligned with Matt's. I mean, I don't think we have data to really support using it, you know, beyond a year. And I do worry about the potential for autoimmune toxicities. And again, they may have been lucky and not having developed them in that year, but you know, I just don't want to really take that risk especially when we really don't know that it's helping.

Dr. Jack West: I would also say that this is a setting where I think we do have some information now as the data mature from Pacific where we see the survival curves at two and three years are not converging. In a way that would suggest that this is just a temporary benefit. And as soon as you stop the therapy, the benefit is gone. There's real hope. And I think almost an expectation that the benefit from that year is sustained, whether that killed the last cancer cell or it has trained the immune system to now sustainably treat the microscopic amount of cancer that exists. But the fact that the curves are just as separate at three years as at 18 months, would lead me to be pretty strong in my recommendation against ongoing indefinite treatment for the reasons you mentioned. And the fact that in stage four disease, we do have patients who are years out who are still enjoying the benefit of no progression, even potentially long after they've discontinued a drug like Keytruda or one of these other immunotherapies.