Case Based Panel Discussion 2019- Lung cancer Unresectable NSCLC

Case Based Panel Discussion – Stage 3 NSCLC Patient with PDL1 Score of 0, Is Immunotherapy Beneficial?

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 approach for a patient with PDL1 score of 0. Would immunotherapy be beneficial?

Dr. Jack West: You have a patient who happens to get testing in the setting of stage three and has PDL1 that comes back as zero. They get through chemo and radiation. We have an unplanned analysis of various subgroups in the Pacific trial that demonstrated a benefit of up to a year of durvalumab Imfinzi immunotherapy after chemo and radiation for stage three. And in that subgroup analysis, the patients with PDL1, the protein associated with more or less risk benefit from immunotherapy. The patients who had zero expression of this protein didn't seem to benefit from durvalumab. How do you use this information when you're sitting down with the patient? Presume they don't have any warning signs to suggest they couldn't, shouldn't get it. Do you present this information? Do you suggest that this is probably not worth their while? Or how do you frame this information?

Dr. Matthew Gubens: I guess I have to admit that at my institution, we don't look. If you leave your head in the sand, you don't have to address this issue.

Dr. Jack West: Don't ask don't tell is an arguable point and that's why I framed it as, but sometimes it's done Surgery, you know, the surgeon well-intended, thinks more information is better or it's reflexively tested or whatever. There's lots of circumstances where it could be

that someone transfers care, but that has that dye has been cast. So yeah, it's now your problem.

Dr. Matthew Gubens: Exactly. And we should say out loud that you're different regulatory agencies have handled this differently. If you are in Europe and you're under the subject of the European medical agency, they didn't approve Imfinzi durvalumab for the zero percenters based on this data.

Dr. Jack West: So that makes it easier for them.

Dr. Matthew Gubens: It makes it easier for the European investigators not to even ask the question, but I think there are two things. One is that it gets into the weeds a little bit. PDL1 is a test that has been, that has come up in many permutations like every company that makes immunotherapy has a different PDL1 test. This company, the cut point they decided to kind of make most of their hay around is 25% higher or lower. And so there's some argument that the 22C3 that a lot of us do in a stage four setting, being a type of PDL testing versus the PDL1 that they did on this trial where the distinguishing ability lower than 25% meaning, can you tell the difference between zero and 5%? It's not quite as clear. Basically my hand wavy answer is I do mention this to patients if I happen to know, I tell them that one part of the study suggested that the time of length of holding the tumor down was a little bit longer. There was a hint toward that, but the survival was a hint toward a little shorter. But these were very small numbers and we kind of talk it through. And I would say that if a patient were more beaten up than average after chemo radiation, I'm less enthusiastic about the durvalumab or Imfinzi, or I'm more likely to stop it at six months if there's some adverse event. But I still offer it. If I had that data in front of me, I'd probably talk this through with the patient. But if they kind of said, Doc, what would you do? I'd have to scratch my head, gulp a little bit. And I probably, again, in this curative setting where I'm just going for the brass ring, I probably actually wouldn't take it personally. But I really would, I'd look.

Dr. Jack West: This is not a setting where there was a harmful effect. It was just maybe these patients don't even get as much as everyone else.

Dr. Matthew Gubens: And I'll be looking, we're hoping that, you know, this is specific. There's like a one through eight. Every other company's doing trials like this. I hope we'll have better data to answer this question when we talk in 2020 and 2021, but that's kind of where I put my foot down.

Dr. Jack West: Well, I think it's fair to acknowledge that you know, one of the concerns is what can you minimize in terms of anticipatory regret? Will you wonder what if, if you don't do it versus if you have. Mille, what's your approach?

Dr. Millie Das: Yeah, I mean I think I, I've had situations of patients where their baseline pulmonary function is not great. They are a little bit beat up after the chemo radiation. And then the consideration of durvalumab or not. If they're PDL1 zero, I think I use that as maybe an additional kind of drop in the bucket against doing the durvalumab. And you know, again, kind of having that discussion is important. And I've actually faced this clinical scenario number of times in recent months and have used that. The other thing that people are starting to look at is this concept of minimal residual disease or MRD testing. So doing that testing in people after they've finished chemo radiation to see if there's any detectable circulating tumor DNA and using that potentially. So kind of similarly to the PDL1 cutoff, you know, if you don't see circulating tumor DNA, would you use that as a reason to not give durvalumab? I don't know. Of course, we don't have answers to that, but in a situation where you're kind of on the fence. There are, I think the PDL1 less than zero, the CT DNA. Whether or not it's detectable, I think those things could kind of be part of that, you know, balance of, you know, should you offer it or not. Again, the risk benefits