Case Based Panel Discussions 2019- Lung Cancer Unresectable NSCLC

Case Based Panel Discussion- Unresectable NSCLC, In a Frail Patient with Competing Risks, Is the Standard Treatment the Best Approach?

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 a frail patient with potential competing risks, and whether the standard treatment of chemotherapy and radiation followed by immunotherapy is the best treatment approach.

Dr. Jack West: In broad practice in the US, and I think even more in the rest of the world. The reality is that a lot of patients don't get concurrent chemo and radiation and then there's a fallout and a lot of patients don't get immunotherapy. Millie, I'm really interested particularly because you're in a VA system that is not a highly selected population of younger, extremely fit patients. Is it common for you to have patients who you think are not strong candidates for concurrent? And I'll say that I worked in a community based setting that's pretty broad range of patients and I moved from giving concurrent cisplatin and etoposide chemo with radiation, which is pretty rigorous to a lot more weekly carbo and paclitaxel. There are data to support that and that is much more tolerable overall. I think it leads me with the question of whether any ambulatory patient who can walk in on their own power is not a candidate for that. But I'm interested in your thoughts cause you probably see some patients who are not doing handstands and olympic candidates here. Right?

Dr. Millie Das: Yeah. I mean, I think as you mentioned, cisplatin, and etoposide is a very difficult regimen. It's a regimen that I'm not frequently giving to patients at the VA, usually due to just baseline hearing loss, renal insufficiency, things like that. But the weekly Carbo Taxol regimen is very well tolerated. I've treated patients in their upper 90, 80s, sorry, even low nineties with the weekly concurrent Carbo Taxol radiation and they've done okay. And one of the great things is that you can try it and then you can, you know, drop it if they don't tolerate it, but it is a pretty good well tolerated regimen that I think the RTOG 0607 trial employed that regimen and the, you know, median survival time was, you know, quite, quite good in that trial. And I think it lends support to that regimen. A lot of us sort of felt that maybe it was inferior to the [inaudible] side regimen, but I feel confident about being able to administer that with a, you know, definitive cure intent. And so most of my patients are able to get the concurrent chemo radiation with a weekly Carbo taxol regimen. There are, I, you know, I've just, in the past few months, I have seen patients who are more kind of, ECOG performance status two bordering on three, where it makes me nervous to give them chemotherapy. They may have had a recent cardiac events, something like that. In that case, I will talk to them about the options. Generally it's good to know up front whether you're going to give a concurrent chemotherapy regimen because the radiation oncologist may want to give a more hypofractionated course of radiation.

Dr. Jack West: Which is a short course of fewer treatments.

Dr. Millie Das: Right. A little bit higher dose. We generally don't give concurrent chemotherapy during those, the shorter, so instead of six weeks of radiation, they may shorten it to two or three weeks. Easier for the patient. We won't give chemotherapy during that. We think cure rates are lower with that approach. But I think, you know, for these patients you have to weigh risk benefits, and most patients in that situation sort of understand that, you know, the chemotherapy may do them more harm than good.

Dr. Jack West: I think it is worth noting that this is a situation where there are competing risks of it's the cancer, but many of these people have bad emphysema, COPD, other medical problems that may limit their probability of surviving several years, and we do want to make sure the treatment isn't worse than the disease. I think that one of the challenges we've had, and this is just my gleaning the data that are not very strong out there is that part of the mixed results we've had with intensifying with additional chemo is that there is such a wide range of the extent of disease called stage three and the health of the patients who have stage three, that some we may be helping and some we may be harming, by turning up the dial into a dangerous range. And so I think at some point you do need to individualize, especially for the people who are on the outer limits. Matt, what's your approach? I mean, is this something that is vanishingly uncommon at UCSF for Patients who are not candidates for concurrent or, and most of these patients are going to be treatable with at least weekly carbo paclitaxel? Or what is your thought

process for say an 87 year old who's PS two, performance status being fragile but treatable?

Dr. Matthew Gubens: Yeah. And also by the way, that 87 year old has some ideas about the therapy they want also. And when you lay out what chemo radiation looks like and what the chance of cure is on the other end of that, it's a shared decision making. I'm not being glib about that. I think there are, patients have very strong feelings about that, but we also see those patients who are just not quite fit enough to do the chemo radiation and not have a lot of toxicity. And so it's just a very personalized decision about whether maybe sequential doing a chemo and then radiation or vice versa. The other kind of variable in the mix is there are patients, again, stage three is such a wide range of patients. There are some patients where our surgeons say, well, I wouldn't operate on them today, but if you did this and shrunk them, maybe I could. So sometimes some of the discussion is actually giving a little bit of chemo and seeing what happens to see if we then decide to do surgery or do chemo and radiation or what have you. So I kind of all of these, stage three is the one tumor that we actually talk about almost all of our patients in a tumor board setting, which we're thankful to have in an academic setting.

Dr. Jack West: Let's take the scenario of a patient who had an initial discussion and was on the bubble for surgery. I really wonder about how to best treat these patients because many patients, many docs feel get it out that, you know, it's always desirable. And we have data in stage three, borderline resectable to say that it's about equal. If you can get people through it to do the surgical approach with a little bit of chemo and radiation beforehand or chemo alone versus doing more intensive chemo and radiation and omitting the surgery. And they're about the same. And it may depend on how extensive the surgery needs to be, but it's not that clear that just because you can do surgery, you should do surgery.

Dr. Matthew Gubens: Totally agreed. And especially in this kind of immunotherapy era where that's changed the number. So if you're already on the fence about it, but if I don't take a patient to surgery, do the, as by all accounts equivalent effectiveness of chemo and radiation, but I've got this kind of, again, brass ring on the other end that has a shot of improving how long it lasts or maybe just maybe curing, that I don't have as an option as an FDA labeled treatment in a surgical situation. Even our surgeons are trying to say, you know, what, take him to chemo radiation and give them some immunotherapy and we'll talk to you later.

Dr. Jack West: I would suspect it depends on the surgeon.

Dr. Matthew Gubens: Probably true too.

Dr. Jack West: But as you said, as we agreed before immunotherapy was on the scene. It was a very marginal, debatable story. And then immunotherapy raises the utility of a nonsurgical approach, which to me would lead me to think that we should tip the scale more toward a nonsurgical approach. And yet there is still this gravitational pull towards surgery. So my real question is, do you think that this has led or should lead to a move away from surgery because immunotherapy tips the scale clearly in favor of a nonsurgical approach for stage three?

Dr. Millie Das: I mean, I think we really don't know. And I think for someone who really wants to have surgery I mean there's just certain patients who are convinced that that's what they want and they want, and if there's any possibility of them having it, I wouldn't tell them not to do it. And again, you know, surgery is kind of a one and done deal. Whereas the immunotherapy, it's a year therapy, right? And there are patients who just don't want to sign up for that.

Dr. Jack West: And I think that the year of an ongoing treatment is a big thing that we shouldn't underestimate.

Dr. Millie Das: It's every two weeks.

Dr. Jack West: Every Two weeks for a year. My patients loved seeing me. But I think it's a very fair point that you've traded. You've now made treatment go from two months or less to a year and two months and that's a big, big change and you've turned it into a chronic management. So, fair point. One variant on that is you have a patient who could go to surgery after chemo radiation or could do chemo and radiation followed by immunotherapy. I have had surgeons or other people who say, well, how about I do the surgery? And then the immunotherapy. Now we don't have data for this. I'll say that, one interesting thing that we need to learn more about is whether extensive surgery and removing lymph nodes decreases the efficacy of immunotherapy. And there's a bit of evidence, though not enough to say much that removing a lot of lymph nodes could be harmful to the efficacy of subsequent immunotherapy. So is this something that if a patient were to ask you about, can I just do surgery and then do the immunotherapy afterwards or the surgeon suggests, get the benefit of both? What's your view about that?

Dr. Matthew Gubens: I'm going to hue to the data that we have and for now really I think the strength of this trial we're talking about Pacific really was the utility of giving immunotherapy fairly close in time after a chemo radiation exposure. And giving immunotherapy after surgery is a whole different question again, whether the nodes are there, what other things we've done to kind of poke the skunk? Like there are agiment trials we say where you give immunotherapy after definitive surgery that we're waiting on results for. So we'll have an answer in a year or two we hope. But I think for now I wouldn't do it off label.

Dr. Millie Das: Agreed. I wouldn't do it outside of the clinical trial.

Dr. Jack West: Okay. Hard to, we'll need to get that clinical trial some day.