Case Based Panel Discussions 2019- Lung Cancer Unresectable NSCLC

Case Based Panel Discussion- Unresectable NSCLC, Should Molecular Tests Be Considered, and Would Outcome Effect Treatment Decisions?

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 option of molecular testing for stage 3 NSCLC, and whether or not the outcome effects treatment decisions.

Dr. Jack West: Hello again, I'm Jack West. I'm a medical oncologist at City of Hope Cancer Center in the Los Angeles area and founder and president of Grace, Dr. Millie Das, Stanford University and the Palo Alto VA and Dr. Matt Gubens at University of California San Francisco in San Francisco, obviously. Thanks a lot. We're going to be talking about the setting of stage three or locally advanced non small cell lung cancer. And just by introduction I would say that it's a common setting that about 30%, somewhere in the range of a third of our patients with lung cancer present with stage three disease. And I think that one of the challenges, the complexities is the range of what is called stage three. That can include just a microscopically involved lymph node in one of the lymph nodes, I'm sorry, in the middle of the chest between the lungs. It can involve multiple lymph nodes throughout the middle of the chest.

They could be quite bulky and sometimes it is appropriate to really consider surgery for some of these patients. But in the majority of patients with stage three disease, they are probably not well-served by doing surgery once you have many lymph nodes involved or more bulky disease. So if you have a patient with multi station, that is many lymph nodes involved end two disease stage three, you decide that this is not a patient well-served by surgery. Do you order molecular tests for this? A setting like stage four we

routinely do, but in stage three, it's not clear whether we would use this information or whether you would order molecular testing. So if you have someone say with an adenocarcinoma, which is one that would have a reasonable chance of having a mutation, do you order it? And think how this might inform your management? Or do you say this is not a setting where that standard don't ask, don't tell. It's only going to complicate things. So what is your approach for a patient who would otherwise be a candidate for chemo and radiation followed by typically immune based therapy now?

Dr. Matthew Gubens: Yeah. So I think that's a really important point that we, in the academic setting, we kind of always want as much information as we can get. And so, I think from our point of view, we're always getting it mostly to kind of triage patients for potential involvement in clinical trials. There's also an element of prognosis. We do know that even stage for stage certain mutations might actually portend better outcomes. But I think another practical reason is, and we'll talk a lot about we're treating these patients for cure. We hope that our chemo and radiation plus or minus surgery, plus or minus immunotherapy is going to cure the patient. But still a majority of these patients will progress. And sometimes it's nice to have this information in our back pocket so that if and when they do progress, we're not starting from scratch and starting that four week clock toward getting those data to get them started on treatment. So for all those reasons, we do tend to get it, but I fully acknowledge that generally I'm not going to use it in my treatment decisions for these patients.

Dr. Jack West: Do you think it should be any kind of standard of care? I mean, what if a colleague out in the community asks you if they should be doing it? Do you say it's an option but not a standard or do you recommend it?

Dr. Matthew Gubens: That's probably how I would pitch it as an option. Not a standard. That's how I would say it.

Dr. Millie Das: That's exactly what I would say. I, you know, I don't think it really informs our treatment decisions right now. Outside of a clinical trial, we did have the NRG oncology trial and open at Stanford where patients with EGFR and ALK, were randomized to receive either, you know, targeted therapy, lead in two months targeted therapy followed by chemo radiation versus just going straight to chemo radiation. So of course, in that context it was important to know whether a patient had EGFR ALK. Although I think that study I think has closed because it is tough to get that information and it's not part of standard practice. And so it's not something I would generally do as or recommend as standard practice. But again, in an academic setting, I think it's useful to have that information. From a practical standpoint, I've asked our pathologist to send molecular testing on any lung cancer specimen just as a reflexive testing. And so I do generally have that information, but I, you know, do I act on it in these patients with stage three disease? No, I generally do not.

Dr. Jack West: Do you have any concerns whether in your practice or for people out in the community that this testing costs money and maybe won't be covered by an insurance?

Dr. Millie Das: I didn't. That's something to consider. Yeah, I think I'm a little bit naive when it comes to that, working in an academic and then also government you know, facilities I don't think as much about that, but I think that, that brings up a great point, especially if it's not going to alter your management

Dr. Matthew Gubens: To cut to the chase. I would never tell a patient to spend $5,000 on these results. You know, we usually get, it either gets forgiven or the university kind of kind of eats the cost, but I completely agree that I wouldn't go out of my way to recommend it because it's not going to change practice in the short term.

Dr. Jack West: So if you had a never smoker with an EGFR mutation that you identified the key trial that we use to guide our treatment for stage three lung cancer, which is called Pacific, gave chemo and radiation, and then follow that up to a year of Imfinzi durvalumab immunotherapy in patients who hadn't progressed. And there's a clear survival benefit. This has become our standard of care. But in a subset analysis, looking at the various variables that seem to be associated with more or less benefit, the patients with an EGFR mutation did not seem to get a benefit. And in patients with stage four disease, the patients with an EGFR mutation often get pretty minimal benefit from immune therapy. Would that inform your decision? You both said that you generally wouldn't use molecular testing to guide decision making, but does this information about the subset of EGFR mutation positive patients lead you to feel that you'd be less enthused about recommending Imfinzi or even consider giving an EGFR inhibitor as consolidation in this setting? Millie?

Dr. Millie Das: Yeah, I mean, I think that that does bring up a very good point. So I think it's a conversation that you have with your patients. And you know, especially when we're not seeing that benefit and it's committing a patient to an additional year of therapy that otherwise they wouldn't necessarily need or be coming in for. So talking to them about this particular subset analysis, I think one of the things that also comes up in these EGFR patients is if they do recur or progress after chemo radiation, and you're going to be offering them a Summerton or Tagrisso. There's some worry about the overlap of them having received durvalumab and Summerton and the risk of pneumonitis in that setting. And I think that that complicates things even more. So. I probably wouldn't recommend the durvalumab as strongly in a EGFR patient if I have that information up front. Again, have a conversation with them about that. And I would also just bring up the concern for the risk of pneumonitis if we were to have to switch to durvalumab.

Dr. Jack West: So to have a thorough discussion and then come out of that as a shared decision about whether to proceed. Matt, what's your impression?

Dr. Matthew Gubens: I think it's a tough issue and warrants a lot of discussion. We have to kind of take a step back and realize that there are only about, I think 44 or 45 patients with EGFR that were recognized on this trial. So we're talking about very small numbers. So I admit that to my patients and I've had this conversation with a couple of patients who had EGFR mutations often these are very savvy patients anyway, their demographics and I've shown them the slide that talks about how these patients did with such a small patient population. It's hard to know what the real answer is and the point estimate meaning kind of if you have to put a number down, how much should they benefit, did slightly favor durvalumab or Imfinzi, but it just was huge, what we call aerobars, kind of a lot of variability that we don't really know the answer.

So the couple of patients I've talked about have chosen to do it, but I think all of these points are well taken that you're committing patients to a year of drugs that, granted it's easier for most patients in chemo radiation, it has real honest to goodness side effects. And one of my EGFRs patients came off for autoimmune diabetes. She will be on insulin for the rest of her life for a treatment that we're not sure improved overall survival benefit. And on the other hand, you know, you're also, this is the one we are looking for a cure here and I think patients are looking for anything that might even marginally add to that cure rate. EGFR numbers don't cure, as far as we know with the data we have. So it's a conversation. But I think it does speak to the fact that we need to be including [inaudible] outpatients in these immunotherapy trials. A lot of the companies that run these trials exclude them.

Dr. Jack West: Study them more systematically than just.

Dr. Matthew Gubens: List numbers. Exactly. I think that's important to you.

Dr. Jack West: You know, you make the very good point that A, these are patients who could be cured without this. I mean, before we were using immunotherapy, people did get cured. It's not as common as we would like, but it's not astronomically low chances. It's maybe one in five at best, one in four, but possible that the survival is better with immunotherapy. And I think because of that, in a high risk situation, it justifies kind of accepting some risk and going for the brass ring. But we do need to not be cavalier about the risks of bad interactions. Like if we are going to be giving Tagrisso afterward if they progress. So these are tough questions.

Dr. Matthew Gubens: And I will say for those patients for generally on durvalumab, on Imfinzi, I will get imaging every three months. But especially of that EFGR patient, I sure want to find that progression. If it's going to happen early, I want to have a chance to wash out the

durvalumab so that I'm even more kind of attentive to that patient and then their progress over that year of immunotherapy.