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Multidisciplinary Approaches & Considerations on Collaborative Care for Patients with HER2m NSCLC

Announcer:
You're listening to *Project Oncology* on ReachMD. This episode is sponsored by AstraZeneca and Daiichi-Sankyo.

Here's your host, Dr. Jacob Sands.

Dr. Sands:
This is *Project Oncology* and I am Dr. Jacob Sands. Joining me to explore multi-disciplinary approaches in the care journey for HER2-mutated, non-small cell lung cancer are Dr. Nicolas Girard and Dr. Jack West. Dr. Girard is a Pulmonologist and Professor of Respiratory Medicine at Versailles St. Quentin University. He's also the Head of Thoracic Oncology at the Institut Curie in Paris. Dr. Girard, welcome to the program.

Dr. Girard:
Thank you.

Dr. Sands:
We're also joined by Dr. Jack West, an Associate Clinical Professor at the City of Hope Comprehensive Cancer Center and the Clinical Executive Director at AccessHope in California. Dr. West, thank you for joining us.

Dr. West:
Thanks. My pleasure.

Dr. Sands:
Dr. West let's start with you. From your vantage point, what are some initial considerations that factor into your assessment of patients with HER2 mutated non-small cell lung cancer? And maybe as a part of that in just identifying these patients?

Dr. West:
Well, I think that it's worth noting that at this time, we don't have an FDA-approved therapy specifically for HER2 mutated lung cancer, but we do have data that I think most of us would consider quite compelling, if we identify a patient who has a non-small cell harboring a HER2 mutation. And this would lead me to certainly consider HER2 mutation as a target you definitely want to find. I would note that we don't need to specifically do a test sending off just for this. But rather, that this just adds to our conviction that broad mutation testing through an NGS platform is the way to go. I would say that was the way to go when we had seven or five, six, seven targets already. But having eight, nine, ten targets with the addition of KRAS earlier this year now with a approved therapy that is effective, and HER2 would just add to that as one more target worth finding. And it doesn't really need to change the workflow if you're including HER2 in the collection of targets that you're looking for, which I would say the vast majority, if not all of these broad platforms are doing. So, to me I would say that I was already convinced that Next Gen Sequencing is the way to go, now, this is just a bit more evidence to support that. And I think we need to move to very broad adoption of this for these patients with advanced non-squamous or advanced non-small cell in general. And I think then there's just the question of if you find it, where does it fit into the treatment plan when we don't have anything that's FDA-approved. But certainly, the data are compelling.

Dr. Sands:
And Dr. Girard, let me turn to you with the same question. How do you approach this particular subtype HER2 mutations and what is your workflow in identifying those?

Dr. Girard:
Well, the situation in Europe is a little bit different than that in the U.S. because majority of academic centers actually do NGS for the patients diagnosed with advanced non-squamous, non-small cell lung cancer. It's part of usually, it's usually done through academic hospital-based platforms. It can be done through commercial panels. But we actually perform NGS on a majority of those patients. HER2 testing is done part of those NGS panels which usually detect pretty well those alterations and this may be in sessions, point mutations, there is some kind of heterogeneity in those HER2, alterations. But NGS has shown it capability to detect those alterations.

Then, I strongly believe that HER2 testing should be part of NGS panels because it's pretty frequent, even if it's probably one or two percent of patients but it's part of those rare alterations that we need to diagnose because targeted agents have shown promise and are currently tested through clinical trials.

Dr. Sands:
And so now, in talking about NGS testing, let's go back to you Dr. West, based on your experience, what, kind of, team structures and care coordination is needed? This is often something I hear is, pathology department and the medical oncology department and a multi-disciplinary plan has developed as far as the workflow. What is your experience within your institution and what are you hearing form around that country?

Dr. West:
I think that many places have adopted a reflex testing strategy, and I think that's a great plan. At our institution, City of Hope, we don't do that, but it really hasn't been an issue just because it is so expected that it's just something that I would say there hasn't been enough of a need for it to incorporate reflex testing. One of the questions around reflex testing is that the pathologist may not have a good sense of the stage of the cancer in question and whether it's appropriate to send off molecular testing for something that could be early stage and more debatable for NGS testing than a later stage. At our center, we work by essentially whoever is collecting data, that is a pulmonologist, or a thoracic surgeon or something and an interventional radiologist knows to get enough tissue whenever possible. So, I think that's one of the biggest issues is just whoever is getting tissue needs to know to not get the least possible to make the diagnosis but the most that is safe and feasible for good molecular testing. I would say that, you know, one of the biggest problems we face in 2021 is that we have all of these effective targeted therapies but NGS is, is woefully under-utilized. And I think that the long turnaround time that can sometimes be the case, especially when you need to send off tissue and you have to get that from another institution or send it to outside labs that is really a challenge. And in that sense, I think in places that have been able to cut that turnaround time by doing reflex testing, great. We just haven't had enough of a shortcoming without it that, that we need it. It's, it's something that is almost universally requested for our patients and, and the whole system is built in anticipation of that.

Dr. Sands:
And Dr. Girard, in your institution, you mentioned NGS testing. What is the care coordination or the workflow in helping to make that happen?

Dr. Girard:
Actually, we are working on two different sites, one is Institut Mutualiste Montsouris which is a center where pulmonologist are doing the biopsies where surgeons are doing thoracic surgery. And we have Institut Curie for the systemic therapies and radiation therapy. So, we are working on two different sites, two different hospitals, but we built this reflex pathway for the bio-specimens and once you have material from patients with diagnosed with non-small cell lung cancer, you have first this rapid testing for EGFR mutations. It's done through a system that is a bio-specimen system. There are other options to do this rapid testing for EGFR because this is the most frequent genomic alterations to be targeted in the first line setting. And then we, so it's done in the pathology lab together with PDL1 assessment and immunohistochemistries and then the materials are shipped to Curie for the NGS, which is done on DNA and we have also a panel for a gene rearrangements done on RNA. So, sent out to what has been said, it takes the whole process takes about three weeks, which is pretty long for a patients just diagnosed with a metastatic non-small cell lung cancer, but this is the only way to have a good clustering of the patients and to make the right choice for the first line treatment. But this is a two-step process because we have this rapid testing for EGFR which is for now the most frequent alteration for which we have a targeted agents in the first line setting.

Dr. Sands:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands and I'm speaking with Dr. Nicolas Girard and Dr. Jack West about collaborative care strategies for patients with HER2-mutated non-small cell lung cancer.

Dr. Girard, staying with you, you've mentioned a quite comprehensive workflow in genomic testing within your institutions, what is your experience around France and further Europe, if you're able to speak to that, as to the workflows? Is this something that you're seeing in other institutions around the country or are there other challenges that you're noting?

Dr. Girard:

Well, in the large academic centers, this is pretty much the same. And we have this clear pathway from the physician in respiratory medicine doing the, the biopsies to the pathologist and then the molecular biologist. And all these people are participating to the multi-disciplinary tumor board. So, this is a way to discuss the management of patients, but also to have a multi-disciplinary team that is aware of the challenges of each other specialty. So, this is how it works. And this is how, an optimal pathway is built within one or several institutions.

But we have also small hospitals who are managing patients with lung cancer because lung cancer is very frequent, and the large academic centers cannot handle all the patients and here this is far more complex. I agree. Because you have sometimes several pathologists and sometimes pathology, is not in the hospital but is outside the hospital and then you have the molecular biology, which is done in another place, and so, if a patient is diagnosed in smaller centers it may take longer time actually to get the, results of NGS and even sometimes in NGS, is not prescribed before first line treatment. Some tests are done for EGFR, maybe for ALK and that's it. So, this is a shame and we need obviously to, to optimize this., I believe that partnership between smaller hospitals and larger academic centers is probably, a key, to optimize those pathways. And another point is that with the,right now we have maybe four alterations for which we do have targeted agents in the first line setting. EGFR, ALK, uh, uh, BRAF and, and ROS1. This is part of the ESMO Clinical Practice Guidelines, but maybe in the upcoming years, we will have more alterations for which, we will have targeted agents in the first line setting and then we will need to have, a testing before choosing the first line treatment. So, at the end of the day, NGS will become more and more mandatory before treating a patient.

Dr. Sands:
And Dr. West, I'll give you the last word on this. You've highlighted the challenges as well as the importance of genomic testing and the effective, testing being done within your institution, what advice would you give to institutions throughout the country about genomic testing? And then adding onto that, you've highlighted NGS testing as HER2 something that, that you would encourage people to specifically be aware of that testing, as well.

Dr. West:
I think we need to change the framework to articulate that broad molecular testing is an expectation of what defines appropriate management of advanced non-small cell lung cancer today, at least for non-squamous disease but arguably more broadly to, all advanced non-small cell. And I think that we need to think of it as if we were to envision someone with breast cancer not getting hormone receptor or HER2 testing. It just is not thinkable. That is part of the workup that must be done. And it's how you characterize the disease. We need to approach lung cancer the same that that molecular testing is part of the workup and if you haven't done an appropriate job. And I think it just needs to be stated, definitively that this is the standard of care. If you're not doing it is sub-standard care. So yes, we need to change our workflows, we need to get more tissue. I think that is a challenge but it is one that in places that are committed to it have adapted over years and we need to bring everyone up to that standard of getting more tissue.

Dr. Sands:
Dr. West, you've highlighted that any HER2-directed therapy at this time is not really FDA approved but there certainly are some trials that we've seen. Dr. Girard, can I ask you what is your experience in treating patients with HER2 and/or your impression of the literature thus far?

Dr. Girard:
Well, actually, this is a subset of patients for which we have actually a several very specific subset of patients because those patients are usually younger than other patients with non-small cell lung cancer. These are preferably never-smokers and actually these patients as they have a tumor with an oncogene addiction, to in my experience they are less prompt to show response to chemotherapy or, end immune checkpoint inhibitors. So, this is a subset of patients, for which we have an aggressive disease, frequent, CNS metastases, frequent liver metastases, and the efficacy of standard options is actually limited. So, this is why we need targeted agents specific to these alterations. There are HER2 directed targeted agents that have been made available for HER2 positive breast cancer. Some of these agents have been, evaluated in patients with HER2 positive non-small cell lung cancer. We have preliminary data, we have retrospective data, phase 2 studies with new compounds. So, this is highly promising and some of the patients actually have opportunities through participating in clinical trials with those agents.

Dr. Sands:
And Dr. West, the same question for your, what has your experience been in treating patients with HER2, mutations and what is your impression of the literature thus far around treatment?

Dr. West:
Well, my experience has been pretty limited just because I haven't had a lot of folks yet on, on trials but I've seen good results in a subset of those patients that at least as a proof of principle that this is a target that, is really worth, trying to get these patients to, center

where they can get on a trial for, for this target. And so, I would say that trastuzumab deruxtecan with a response rate in the 60% range is terrific. I think that we need to get a broader experience with that just to corroborate that and to also clarify the optimal dosing and toxicity issues. I think interstitial lung disease is a question that we need to clarify and I do note that the dose in the breast cancer population where it's FDA approved is lower than in the tested one for trastuzumab deruxtecan in in lung cancer. But I think that any time when you're seeing response rates in the 50 percent or higher range, it's remarkable and absolutely worth trying to both identify the target and get the patient to somewhere where they can avail themselves of a clinical trial with one of the agents targeting this.

So, that's my overall perspective on it. I do think that right now, while it is true, I certainly agree with Dr. Girard that these folks have not in general had impressive results with the therapies we have. They're relatively understudied. I do think that it will be a very good thing for the field to dedicate more study just to this population to better characterize. My general default has been to favor standard of care therapy least until we have more, more study of this population. But I think it is overwhelmingly worth identifying the target and directing patients to wherever they can go to get on a trial with a promising agent against, HER2.

Dr. Sands:
With those thoughts in mind, I want to thank my guests Dr. Nicolas Girard and Dr. Jack West for sharing their perspectives on genomic testing and caring for patients with HER2-mutated non-small cell lung cancer. Dr. Girard, Dr. West, wonderful having you both on the program.

Dr. West:
Take care, folks.

Dr. Girard:
Thank you.

Announcer:
This episode of *Project Oncology* was sponsored by AstraZeneca and Daiichi-Sankyo. To access other episodes in this series, visit ReachMD.com/Project-Oncology, where you can Be Part of the Knowledge. Thanks for listening!