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Optimizing Treatment Pathways in NSCLC: The Role of the Multidisciplinary Team

Announcer:
You're listening to *Deep Breaths: Updates from CHEST* on ReachMD. This program is produced in partnership with the American College of Chest Physicians and is sponsored by AstraZeneca. And now, here's your host, Dr. Gerard Silvestri.

Dr. Silvestri:
This is *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Gerard Silvestri, a pulmonologist and the Hillenbrand Professor of Thoracic Oncology at the Medical University of South Carolina. Joining me today to discuss the importance of multidisciplinary collaboration in non-small cell lung cancer are Drs. Jessica Donington, Mariam Alexander, and Anurag Singh.

Dr. Donington is a Professor in Surgery and Chief of the Section of Thoracic Surgery at the University of Chicago.

Dr. Donington, welcome to the program.

Dr. Donington:
Hello, Gerard. Excited to be here.

Dr. Silvestri:
Also joining us is Dr. Alexander, who is an Assistant Professor of Medicine and Medical Oncology at the Medical University of South Carolina.

Dr. Alexander, thanks for being here.

Dr. Alexander:
Thank you for having me, Gerard.

Dr. Silvestri:
And finally, Dr. Singh is the Director of Radiation Research, Director of the Head and Neck and Lymphoma Radiation Services, and the Associate Dean of Graduate Medical Education in Radiation Medicine at Roswell Park Comprehensive Cancer Center in Buffalo, New York.

Dr. Singh, it's great to have you with us.

Dr. Singh:
Thank you, Gerard.

Dr. Silvestri:
So, Dr. Donington, let's start with the surgical perspective. How do you define resectability in non-small cell lung cancer, and what surgical criteria guide your evaluation? Also, what's the process for tissue acquisition?

Dr. Donington:
So, the concept of resectability has become a pretty hot topic as of late, and that has really happened with the new trials and all the excitement around the chemo immunotherapy.

Resectability is based really in two realms; it's both technical and physiologic, typically. So, technical: can I perform an R0 resection? That's one of the central questions in resectability. And the physiologic question is: can the patient tolerate what I need to do to them?

So, we could probably take tumor out of anybody, but will the patient live through it—those are the two central questions.

More nuanced questions have to do with things like the value of pneumonectomy in locally advanced lung cancer and operating in patients who might have multi-station N2 disease. That's where a lot of the nuance comes, and there's not universal agreement on what's resectable and not resectable. But I think the technical part really has to do with probably, the nodal involvement and the bulk of that, and then obviously, the physiologic depends so much on cardiopulmonary health.

As for biopsies, most of my tissue acquisition at this point is done with my interventional pulmonologists. With the advent of robotics and navigational bronchoscopy, the ability to biopsy the primary tumor and the lymph node staging all in one setting has really become a very attractive thing both to me and my patients. And I also believe that a good interventional pulmonologist is an excellent tissue steward, which is so important now as knowing the molecular makeup of the tumor is essential in how we talk about treatment, even in resectable patients.

Dr. Silvestri:
I just want to ask you, when you talked about lymph nodes and the extent of mediastinal disease, are you more likely or less likely to offer a neoadjuvant approach for patients with single lymph node disease or single station disease versus either multi-station or bulky disease? Or does that not really come into your mind as you're thinking about these patients?

Dr. Donington:
That's a hard question, but I think the bulk of nodal disease tells us whether something is technically resectable. But I tell my patients very clearly that any nodal disease is a marker for micro metastatic spread. I call those lymph nodes the gatekeepers. And I say, if a tumor cell got to a node, there's a chance that the tumor cells are out somewhere else, and we just can't see them yet.

I think the more nodes that are involved, the greater that risk of micro-metastatic disease. I don't know that the more nodes involved necessarily make someone more or less resectable, to tell you the truth, until you get to the line of N3 disease. But I do think their prognosis is worse because, again, the more nodes involved, the greater risk for micro-metastatic disease and distant failure.

So, I do think that it's that reason that all 3A patients get an induction approach no matter where they're treated. And yet when we go into the N1 disease, there are people who hem and haw, do I need to give induction therapy? In my clinic, the answer is yes, but that's not universal worldwide for sure.

Dr. Silvestri:
Thank you.

I'm going to turn to you now, Dr. Alexander. How do treatment pathways differ for patients with molecular drivers, like EGFR and ALK mutations, compared to those without actionable mutations?

Dr. Alexander:
Thank you, Gerard. So I want to remind everybody that after surgery, four cycles of platinum-based chemotherapy was the standard of care for 20 years, but we now have significant changes over the last few years. We now do biomarker testing to decide if patients are candidates for any targeted therapy after surgery.

So patients with EGFR-mutated lung cancer don't usually respond to immunotherapy. We have the ADAURA clinical trial that randomized patients with early-stage disease who have EGFR mutations to a targeted therapy called osimertinib versus placebo after surgery and chemotherapy. And the overall survival benefit at five years was 88 percent with osimertinib and 78 percent with placebo. And this was regardless of whether they got chemotherapy after their surgery or not.

And for patients with ALK-rearranged lung cancer, the ALINA clinical trial randomized patients with early-stage disease to alectinib versus chemotherapy. And they found that patients who received oral alectinib after surgery significantly benefited compared to those that received chemotherapy.

So in patients that have no driver mutations or who have mutations that respond to immunotherapy, we can either give immunotherapy and chemotherapy after surgery, or we can move the chemo immunotherapy to before surgery. So for the neoadjuvant setting, we have multiple clinical trials that show benefit of the chemo immunotherapy before surgery. You might have heard of these—Checkmate-816, Keynote-671, GN Checkmate-717, and NEOTORCH.

Just to briefly summarize the Checkmate-816 trial, patients got three cycles of chemoimmunotherapy versus chemotherapy before their surgery in early stage disease, and the proportion of tumors that have disappeared—the PATH CR rate—was 24 percent compared to 2 percent for chemotherapy alone. The final OS also favored neoadjuvant chemo immunotherapy. There was a hazard ratio of 0.72, with 65.4 percent of patients alive at five years compared to 55 percent with chemo alone.

There was another trial called Keynote-671, where four cycles of chemo immunotherapy were given before surgery and then one year of adjuvant immunotherapy. And that was also a very strongly positive trial with a hazard ratio for overall survival of 0.72.

So what the field is trying to do right now is to figure out who needs this adjuvant immunotherapy. And what we're finding so far is that patients who don't have that pathological complete response don't do as well as those who have had.

So, overall, what I want to say is that these decisions are so critical and have to be made on initial diagnosis. And I just want to reiterate that it is so crucial for that early molecular testing with that initial biopsy since the management completely changes.

Dr. Silvestri:
Thank you.

A question for Dr. Singh—when patients come to a multidisciplinary visit prior to embarking on neoadjuvant treatment, what input is important from the perspective of radiotherapist, particularly given the fact that if all goes well, you won't really participate in the care of these patients?

Dr. Singh:
Well, unfortunately, what we have to tell patients is that statistically, most of the time, everything doesn't go well. And most patients with advanced disease end up needing radiation therapy, and that could be for a variety of reasons, including the ones that Dr. Donington was talking about—maybe after the induction chemotherapy, they're not quite fit enough for surgery. Or unfortunately, maybe there was disease advancement. Or either the patient or the surgeon has changed their mind.

And so the combination of these factors leads to the vast majority of patients with stage three disease getting both chemotherapy and radiation as their definitive management.

Dr. Silvestri:
So I'll just throw this out to each one of you. Everyone should have a multidisciplinary visit before the decision on whether they get adjuvant or neoadjuvant? And that multidisciplinary visit should include a pulmonologist, a thoracic surgeon, a medical oncologist and a radiotherapist in a perfect world?

Dr. Singh?

Dr. Singh:
In a perfect world, absolutely. It's a very complicated decision matrix and input from multiple sources is very important.

Dr. Silvestri:
Great. Dr. Alexander, same?

Dr. Alexander:
I completely agree with that.

Dr. Silvestri:
And Dr. Donington?

Dr. Donington:
I agree. In a perfect world, yes. Even in my imperfect world, we discuss all these patients with everybody first.

Dr. Silvestri:
For those just tuning in, you're listening to *Deep Breaths: Updates from CHEST* on ReachMD. I'm Gerard Silvestri, and I'm speaking with Drs. Donington, Alexander, and Singh about how we can collaborate in non-small cell lung cancer care.

So, Dr. Donington, let's zero in on the importance of the thoracic multidisciplinary team. How does collaboration ensure patients get to the right treatment at the right time and what roles are essential to this team?

Dr. Donington:
The multi-team in lung cancer has grown a little bit in recent years, and maybe some of the roles of some of the people we used to think of as supporting have really increased.

So I think the central portions of a team include thoracic surgery, thoracic medical oncology, and radiation oncology, but we've really added pathology as being so central and so important to this, and interventional pulmonary. Those two specialties are in the center of my tumor board because tissue means so much, and molecular testing for all of our specimens.

Now, we also have radiology as a very central part in trying to interpret some of these difficult scans, especially in patients who have

undergone treatment. But I think that's the core group anyone has to have. And then we start to think about things like rehabilitation and nutrition as added benefits that you might get within a cancer center but are challenging in the real world.

Dr. Silvestri:
How about our nurse navigators who help coordinate all these things? How important do you think those are?

Dr. Donington:
I think they're so important. This whole process has gotten really complex. When we look at the neoadjuvant protocols that we talked about, or peri-adjuvant, we're talking about patients who are going under active treatment for 18 months and changing hands with three or four different practitioners keeping track of them and making sure that they don't fall off in between. This really requires somebody whose entire job is just following the path and making sure the patients don't get lost. And so I think the navigators are much more important than ever.

Like I said, this is very personalized approach to treatment, but that means everyone's not on the same path. How do we keep them on the correct path for them? It doesn't just happen; it's work.

Dr. Silvestri:
Yes, I couldn't agree with you more.

Now, from your vantage point, Dr. Alexander, what are the biggest barriers to effective referrals and multidisciplinary integration that you've seen in your practice?

Dr. Alexander:
So the biggest barriers is the patient is actually in a system that does not have that multidisciplinary care in the same building, where they can be quickly seen by multiple specialists, get their biomarker testing done, and have a final plan quickly. The goal is not to delay their surgery any more than it needs to be.

This can be even further complicated if the health records are also fragmented and there's no central navigator to coordinate this patient's journey. All this can lead to significant delays in care and patients can get lost in this system. They may receive inappropriate treatments, such as immunotherapy in a neoadjuvant setting, where they actually have an EGFR/ALK positive cancer, or they may not have had the opportunity to receive immunotherapy upfront when that could have been the best treatment for them.

So somebody needs to be the quarterback for these patients once they get into a system at any entry point. And I feel like most of the time that quarterback is the pulmonologist, who first needs to ensure that the patient has an adequate biopsy with enough tissue for the studies, and then they are seen by all these specialists, such as the surgeon, medical oncologist, and radiology oncologist to get the best multidisciplinary care.

Dr. Silvestri:
Before we wrap up, Dr. Donington, I'd like to ask you one last question. What are some actionable steps that clinicians can take to strengthen the MDT or referral process in their own setting?

Dr. Donington:
It's hard because it's very much dependent upon what your setting looks like. I think one thing that we have found really helpful, both in my university practice and at a couple community hospitals where I practice too, is just making sure communication is open. And I have worked on setting up text chains. You make sure that you're not just texting with your oncologist, but maybe all four or five of those central people who need to know what's going on. I use the phone a lot more, and a lot of our medical records have chat functions where a whole group can go on. The insights can come very quickly. But I think we just have to be willing to do that.

The other thing is setting up those tumor boards. Making sure that your institution, if you have a big enough body of lung cancer patients, is doing a lung-specific tumor board as necessarily as needed. And in my institution, we're moving to two a week to make sure no one's getting delayed because we just have too much to do in one day and we don't want it to wait another seven.

Dr. Silvestri:
I completely agree, and I think communication is the key. And whatever method you use, communication between those service lines is really important.

And I would say the pathologist, as was mentioned before, is so important, and they seem to be left out of the conversation a lot, and so I always tell people go buy a cup of coffee, go down to the bowels of the hospital where they always seem to be and find them. They're more than happy to talk to you, and then they can talk to you about what their challenges are, what tissue they need, and if you could do reflex testing to get biomarker results in a quick fashion.

But it all comes down to communication. And we're lucky in larger institutions to have those people in the same place at the same time, and we have a little bit more time than maybe a busy practitioner to be at those tumor boards, whereas they're dealing with, for example, a community oncologist that has to see breast cancer and lung cancer and colon cancer, and they all can't get to the tumor board at once. So I think communication is absolutely the key.

And the last thing is, I don't think any of us in academia, in large cancer centers, want to "steal patients." And so for our communities, what we'd like to see is just communication between finding someone who has this expertise at a larger center and maybe at least talking to them about helping with the care of those patients. I think we're all here to help our patients do better.

I want to thank my guests, Drs. Jessica Donington, Mariam Alexander and Anurag Singh, for joining me to share their perspectives on multidisciplinary care for patients with non-small cell lung cancer. Dr. Donington, Dr. Alexander and Dr. Singh, thank you so much for being here.

Dr. Donington:
Gerard, thank you. It was a great discussion and thank you to CHEST.

Dr. Alexander:
Thanks for the great discussion, Gerard.

Dr. Singh:
Thank you very much, Gerard.

Announcer:
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