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Creating Targeted Treatment Pathways Driven by Genomic Makeup & Cancer Type

Announcer:
This is ReachMD, and you're listening to Closing the Gaps in Non-Small Cell Lung Cancer, sponsored by Lilly.

Here's your host, Dr. Paul Doghramji.

Dr. Doghramji:
Recent research in non-small cell lung cancer space has brought to light the ability to use a patient's cancer type and genomic makeup to create a targeted treatment plan. So how can we use this improved knowledge to our advantage and what does it look like in practice? Welcome to Closing the Gaps in NSCLC on ReachMD. I'm Dr. Paul Doghramji and joining me today is Edward Kim, who is the Chair of Solid Tumor Oncology and Investigational Therapeutics and the Donald S. Kim Distinguished Chair for Cancer Research at the Levine Cancer Institute Atrium Health in Charlotte, North Carolina. Dr. Kim, welcome to the program.

Dr. Kim:
Hi. Thank you. It's my pleasure to be here today.

Dr. Doghramji:
Wonderful. So, to set some background for us here, can you help define for us targeted treatments in the context of non-small cell cancer?

Dr. Kim:
Yeah. In lung cancer especially, we have seen quite a renaissance in targeted therapies with corresponding biomarkers. If we think back 15 years ago, we were giving platinum-based doublets to anyone who was coming in who was able to tolerate receiving the chemotherapy and that made clinicians feel very helpless and certainly made the patients feel even more so. We have evolved quickly with the use of genomic testing, biomarker identification, and finding corresponding therapies, many of which are oral therapies, which are more convenient to take, patient's that have different side effects profiles, and now we're able to, as a standard, test patients who are diagnosed with non-small cell lung cancer, assess their biomarker status, and give them the appropriate oral targeted therapy. Now what is great is this is really a paradigm that was started in breast cancer and, for decades, patients with breast cancer were tested for their hormone status or HER2 status and given the appropriate targeted therapy up front, and that's really what we're still striving for in the care of patients is to make sure we do this biomarker testing up front and identify those unique features.

Dr. Doghramji:
Very interesting targeted treatment. So, what are the currently known and understood therapeutic targets for this cancer based on known mechanisms of disease?

Dr. Kim:
There are several and it seems like, especially in lung cancer, it continues to grow. The epidermal growth factor receptor, EGFR, is the first and still the most prevalent. We have other targets now such as ALK, ROS1, BRAF just like in melanoma we test as well as, even in some cases, PDL1, to help us identify a subset of patients that may benefit from a single agent immunotherapy. We also test, more recently, TRK fusions, which is a very rare fusion that occurs but now has a drug that is FDA approved, two drugs actually that are FDA approved for this very rare indication and this continues. So, we hope to add a few more biomarkers to this list in 2020 and their corresponding treatments. But, at a minimum, these markers need to be done up front in patients.

Dr. Doghramji:

Alright. So, let's consider the emerging targets then Dr. Kim, what is being investigated and what looks particularly promising?

Dr. Kim:
There are multiple areas being investigated in non-small cell lung cancer and I think it's good because in the past, we used to think that if a marker had low incidence, then many companies didn't want to pursue that area of research because there wouldn't be that many patients, but even a small percent in a cancer type like lung cancer, which has so many cases, is going to be a large number of patients. One of those is KRAS. KRAS is being looked at very closely. It's been a pretty prevalent marker but there hasn't been a lot of therapy that has worked and, in fact, KRAS mutations have been a poor prognostic factor. Now there are some treatments on the horizon that I think are going to make an impact. We're also looking at things like MET exon-14 mutations; there are drugs that are targeting this particular rare mutation, less than 5% of patients with lung cancer, and perhaps they may also make a difference. You have things that are related to the EGFR family like exon-20 insertions where we're finding, again, drugs that may have specific targets to these unique mutations, again, a rare subset, and then we also look at areas like RET. RET is an area, just like I talked about BRAF, which was first used in melanoma and also in colon cancer, now we have the treatment in lung cancer. RET had its origins in thyroid cancers and now is being actively tested in patients with non-small cell lung cancer and we're seeing some very impressive results.

Dr. Doghramji:
Very interesting. Dr. Kim, you said that these medications are oral medications, how has it been received by patients and what's been the side effect profile?

Dr. Kim:
Yeah, they're not all oral, but the majority of them are oral and that's, in fact, been very nice because what we like to see is we want to give the patient some freedom. One of the things that really makes reminds you that you have cancer and you're being treated is an IV, or having to sit at an infusion unit while getting the drugs, by having pills, gosh, you know, people who don't have cancer take different types of oral medications and so, patients have that freedom; they can go out and around. The side effect profile is different. It doesn't suppress your immune system, generally, so you're not going to see those complications of immune suppression with fevers, and neutropenia, and other aspects. So, again, they're different. Certainly some of them can be severe but, all in all, the side effect profiles have been much more favorable for patients with these oral medications.

Dr. Doghramji:
For those of you just tuning in, you're listening to Closing the Gaps in NSCLC on ReachMD. I'm Dr. Paul Doghramji and I'm speaking with Dr. Edward Kim about how we can create targeted treatment pathways driven by genomic makeup in cancer type. So, Dr. Kim, we spoke a bit earlier about emerging therapeutic targets but now let's focus on cancer genotyping. What do our current understandings for the genetic basis of non-small cell cancer inform us about new avenues for treatment?

Dr. Kim:
It's a mandate right now and it's not being done in 100% or even 95% of patients. Again, 15 years, 20 years ago, we didn't do any of this testing whether it was blood testing or tissue testing to look for genetic alterations. Now, it's an absolute requirement in several different tumor types in lung cancer especially prominent in that. In order to make the best informed treatment decision, the best precision medicine decision for a patient, you have to order a test. There are all different types of panels; some are larger, some are smaller. It's a matter of just getting a test done and getting the results and using them to drive the treatment choice. And, in about 40% or more of our patients in lung cancer, you will find an alteration that you can target with a specific targeted therapy that's not just a chemotherapy. So, it is of the utmost importance to do that. There have been hurdles such as sometimes these tests are send-outs so it can take two to three weeks to get the results back and, you know, when people are diagnosed with lung cancer, they are very panicky and they can't wait that long, but it is important to have that information just as important as making a pathological diagnosis to really make the best decision for treatment.

Dr. Doghramji:
Understanding the heterogeneous nature of these solid tumors, how do we take this factor into account when considering these targeted therapies?

Dr. Kim:
These genomic tests drive our treatment decisions. And so, it really has to do with matching them up. And there are times the majority of patients still will not have a driver mutation or a targeted abnormality and so they will receive a standard therapy and these days the standard therapy for those patients who are eligible is a combination of chemotherapy with immunotherapy. Some people would say that's a consolation prize, some people would say that's actually great because immunotherapy has been getting a lot of press and certainly the results have been very impressive, combining chemotherapy with immunotherapy, especially in non-small cell lung cancer. But, again, chemotherapy is always a little more rough than receiving oral therapy and so we want to go with, again, the least amount of

side effects with just as much, if not more, effectiveness. And so, it really is a very straightforward paradigm. There shouldn't be much interpretation that's needed here.

Dr. Doghramji:
Can you run us through the factors regarding cancer type that we should keep in mind when initiating therapy?

Dr. Kim:
Non-small cell lung cancer is divided up into pretty much adenocarcinoma and squamous cell carcinoma. That is, as far as histologic subtypes and then if you go a little more macro, it's non-small cell versus small cell. The targeted treatments pretty much reside in the adenocarcinomas or the nonsquamous non-small cell lung cancers. This is where we have found most of the driver mutations. We have found things like PDL1 in the squamous side and then more so, as we do more testing, we're finding more of these types of alterations in the squamous histology. We haven't found too many in small cell, and so, small cell has still been very challenging over the decades but, again, you know, it's less important to try and find selected patients with different histologies or characteristics. We used to do that in the early 2000s. For instance, if you were an Asian, female, or never smoker, you should definitely test because they have a high likelihood of having an EGFR mutation. We found equally that people who smoke do have EGFR mutations and people of other ethnic origins, whether it's Caucasian or African-American also have EGFR mutations and so we shouldn't really be looking to um select which patient groups should get tested, we should be testing all of them.

Dr. Doghramji:
That's very interesting. Dr. Kim, lastly, is there anything you'd like to share with our audience today?

Dr. Kim:
Yeah, I think one big message to the audience is is that there's been tons of progress, just earth-shattering progress in the treatment of non-small cell lung cancer. We have still a ways to go, but patients are now living longer and living better and that's really the key and it's been driven by precision medicine, especially centered in non-small cell lung cancer. If you're a patient or know someone, a family member, make sure you get genomic testing done, that's number one, and then use that information to drive treatment. Yes, you could receive immunotherapy and that's a great therapy to be on, but there may be other options that are more genetic matches based on what treatment we have and what's inside your individual tumor. So, I think you have to be your best advocate, your own advocate, when you're going through this.

Dr. Doghramji:
Very informative and promising comments, Dr. Kim, for us to think as we come to the end of today's program. I want to thank my guest, Dr. Edward Kim, for joining me today. Dr. Kim, it was great having you on the program.

Dr. Kim:
Thank you. I appreciate it.

Announcer:
This program was sponsored by Lilly. To revisit any part of this discussion and to access other episodes in this series, visit ReachMD.com/NSCLC, where you can Be Part of the Knowledge. Thanks for listening.