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Current Guidelines and Real-World Evidence for ROS1 Testing in NSCLC

Announcer:
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Dr. Aggarwal:
Hello, I'm Dr. Charu Aggarwal. I'm an Associate Professor for Lung Cancer Excellence at the University of Pennsylvania Abramson Cancer Center. Today, we'll talk about current guidelines and real-world evidence for ROS1 testing in non-small cell lung cancer.

As we know, molecular testing in the management of patients with non-small cell lung cancer is extremely important. ROS1 is one of the molecular aberrations that we must look for when we come across a patient with a diagnosis of non-squamous non-small cell lung cancer. But unfortunately, even after recognizing that this is an important diagnostic method, we find that practices in the United States are variable as they relate to molecular testing. Additionally, we know that there can be several different ways to test for ROS1. There are different modalities that we'll talk about a little bit later that may also complicate this issue and lead to the problem of undertesting.

So, before we go to testing practices, what is ROS1? ROS1 rearrangement is a molecular aberration that can be genomically targeted, therapeutically targeted with available drugs.

Testing for this is recommended currently for all patients with non-squamous non-small cell lung cancer or those with a squamous histology who may not have enough of a significant smoking history. It can be tested by using a FISH Break Apart Probe. IHC can be used for ROS1. And then finally, sequencing assays such as next generation genome sequencing, as well as targeted PCR can also look for ROS1 fusions. If we were to consider the whole spectrum of ROS1 fusions, they are present in about 1 to 2% of all non-small cell lung cancers. So, we really have to look for them and make sure that we're doing the correct testing.

So, there are advantages and disadvantages of the different approaches. Immunohistochemistry is a very easy way to look and screen for IHC. And I emphasize this, that it may just be a screening tool, but there is lack of global consensus on how to act upon a, quote unquote, positive result. And I think even if we find something that's positive by IHC, we must confirm it by other methods. PCR may be another method, it's highly specific, short turnaround time. However, RNA integrity can be an issue when it comes to PCR. And it may or may not be able to give us an accurate rate.

What we do recommend is next generation gene sequencing that allows for simultaneous testing of many predictive biomarkers, it does have a longer turnaround time. But if we especially combine DNA and RNA sequencing, we can ensure that we are looking for all of the ROS1 fusion changes that may be present in a patient's tumor.

FISH can also be used, it's highly specific, it's sensitive, it has a short turnaround time, but sometimes it requires a knowledgeable interpreter, as well as the molecular cytogenesis to be able to give us an accurate answer. In my practice, I prefer to use next generation sequencing with simultaneous RNA sequencing to be able to detect these rare fusions.

It's important to recognize that there are several different TKI therapies for ROS1 rearranged lung cancer. Going back several years

now, crizotinib was first studied for this disease with significant responses across all studies, response rates have been above 70%. But now we have entrectinib, as well as repotrectinib, and all three of these drugs are actually recommended, preferred first-line treatment options for metastatic ROS1 rearranged non-small cell lung cancer.

If we find that a patient had a mutation or rearrangement discovered during therapy, our options are to either continue the chemotherapy and then switch over to the TKI in the maintenance phase, or it's completely appropriate to also interrupt the current therapy and then switch to one of these agents.

As is inevitable unfortunately, progression does happen, especially in the setting of metastatic disease. And there's several different ways to approach progression. It could be either treating with definitive therapy in case of oligoprogression. This can be either in the brain; so, if patients have asymptomatic or new brain metastases, these can be really treated with radiation alone or changing to systemic therapy.

Again, I think changing from a first generation TKI to a later generation TKI is absolutely fine and has the data to be able to do it. There are multiple options in the case of systemic therapy, going to later generation TKI or even going to systemic therapy including chemotherapy.

So, in summary, ROS1 fusions represent an immediately therapeutically targetable subset in lung cancer. Imperative to test for these alterations, response rates up very high. And then many options exist for first-line therapy in treatment for progression, including for those patients with CNS disease.

Thank you for watching.

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