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Investigating Emerging Therapies in HER2m NSCLC

Announcer:
Welcome to *Project Oncology* on ReachMD. This episode is sponsored by AstraZeneca and Daiichi Sankyo. Here's your host, Dr. Hector Chapa.

Dr. Chapa:
This is *Project Oncology* on ReachMD, and I'm Dr. Hector Chapa. Joining me to explore emerging therapies in HER2-mutated non-small cell lung cancer is Dr. Sandra Misale. She is Research Associate at Memorial Sloan Kettering Cancer Center. Dr. Misale's research focuses on the connections between genetics and molecular pharmacology to develop personalized cancer therapies. Dr. Misale, welcome to the program.

Dr. Misale:
Thank you so much for having me.

Dr. Chapa:
Let's begin by taking a look at the treatment landscape for HER2-mutated non-small cell lung cancer. Dr. Misale, what are some current therapeutic options for these patients?

Dr. Misale:
Current therapeutic options for HER2 altered, non-small cell lung cancer patients are mainly chemotherapy, but also there are new emerging therapies on the horizon that are in clinical testing right now.

Dr. Chapa:
And, having said that, what are some of the primary challenges that you've seen with these treatment options?

Dr. Misale:
One of the primary challenges with this treatment option is that it's still not really well-understood whether chemotherapy is the best option for these patients. Some studies suggest that it'sHER2-mutant lung cancer can benefit from this kind of treatment, but other studies suggest the opposite, so that means that we still don't know exactly what is going on or what is best chemo regimen for this kind of patients.

Dr. Chapa:
For those of you just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Hector Chapa, and I'm speaking with Dr. Sandra Misale about therapies for HER2-mutated non-small cell lung cancer. So Dr. Misale, now that we've reviewed the current landscape, let's take a look at what's on the horizon. So what are some emerging treatment options for HER2-mutated non-small cell lung cancer, and what are they targeting?

Dr. Chapa:
And so, Dr. Misale, now that we've reviewed the current landscape, let's take a look at what's on the horizon. What are some of the emerging treatment options for HER2-mutated non-small cell lung cancer, and what are they targeting?

Dr. Misale:
So, the emerging treatment options that are currently in clinical testing are small molecule inhibitors, that can target the tyrosine kinase domain of this protein of HER2, but also other bigger molecules that are monoclonal antibodies that are conjugated with chemotherapies. And they are called antibody drug conjugates, or ADC.

Dr. Chapa:
Okay. And now that we've established that, that leads me to my next question. Can you tell us a little bit more or elaborate a little bit more, on their specific mechanism of action?

Dr. Misale:
Sure. So both these two approaches are actually targeted therapies against HER2 itself. We can have patients that harbor HER2 mutations, or HER2 amplification. In both cases, these drugs are effective at least in our technical model, and in the clinical testing right now.

In general, the tyrosine kinase inhibitor can bind the HER2 from inside of the cells, and that causes the inactivation of the receptor, and therefore the inactivation of what the receptor sustained at this proliferation and survival. On the other hand, when we talk about antibody drug conjugates, we have an antibody that it's the specific for HER2, so targeted exclusivity to HER2, sparing the cells that don't have HER2 on their surface. So, from the outside, it does cause the inactivation and most importantly, the internalization of this receptor inside the cells, and this basically starts a process that ends to the degradation of the receptor. So that also basically stops cell proliferation because cells are not sustained by HER2 activity anymore.

Dr. Chapa:
That's really incredible. Very targeted and very specific. So, what about their safety profile? What can you tell us about that?

Dr. Misale:
So, in general, every targeted therapy has some side effects and toxicity in patients. So it depends on the context, or on the side effect that a patient that can experience. There are many ways that clinicians always use to manage the toxicity. In this specific case, the side effects that can happen after anti-HER2 therapies are several, but most of them are actually manageable, and the patient can still benefit from this treatment. The tumor can shrink, and they can live usually a pretty normal life.

Dr. Chapa:
Well, having said that, that brings me to my next question, and probably most important. As this landscape continues to evolve, Dr. Misale, how might these novel therapies improve patient outcomes?

Dr. Misale:
Of course, these new therapies are always in continuous evolution. We are working to test new molecules, to improve the efficacy of the current molecules, to also understand what are the mechanisms of resistance that some patients can evolve doing the treatment, so that these drugs are initial effective, but then they don't work anymore. So, all of these open questions are part of our work as researchers, and clinicians as well, in order to understand and move forward to always better understand what are the molecular mechanism and how to improve the patient's life.

Dr. Chapa:
Well, with that being said, I look forward to seeing the impact of these novel new therapies. And with that, I wanna thank my guest, Dr. Sandra Misale, for joining me to share her insights on emerging therapies for HER2-mutated non-small cell lung cancer. Dr. Misale, it was great having you on the program.

Dr. Misale:
Thank you so much.

Announcer:
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