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Pathways to Evolving Personalized Medicine in Gastric and GEJ Cancer: An Overview of Current Established and Emerging Biomarkers

Announcer:

Welcome to ReachMD. This medical industry feature, titled “Pathways to evolving personalized medicine in gastric and gastroesophageal junction cancer,” is sponsored by Astellas. This program is intended for US physicians.

Your host is Dr. Charles Turck.

Dr. Turck:

According to the American Cancer Society, in 2022, patients diagnosed with gastric cancer accounted for 1.4 percent of all new cancer diagnoses in the United States, with a five-year overall relative survival rate of 33 percent. Learn how biomarkers play an important role in gastric cancer and how personalized medicines can create more targeted therapies to improve patient outcomes.

This is ReachMD, and I’m Dr. Charles Turck. Joining me to discuss the pathways toward personalized medicine progression through diagnostic biomarkers are Dr. Nataliya Uboha and Dr. Kristina Matkowskyj.

Dr. Uboha is an associate professor in the Department of Medicine at the University of Wisconsin School of Medicine and Public Health, and her focus area is gastrointestinal malignancies.

Dr. Uboha, it’s great to have you with us!

Dr. Uboha:

It's a pleasure to be here.

Dr. Turck:

And Dr. Matkowskyj is a professor in the Department of Pathology and Laboratory Medicine at the University of Wisconsin School of Medicine and Public Health who specializes in gastrointestinal pathology. Dr. Matkowskyj, welcome. Also, great to have you with us.

Dr. Matkowskyj:

Thank you for having me.

Dr. Turck:

Let’s start with you, Dr. Uboha. Would you walk us through the current and emerging biomarkers in the gastric and gastroesophageal junction, also known as GEJ, cancer space?

Dr. Uboha:

Certainly. Well starting off, gastric cancer and GE junction cancers are difficult to treat malignancies, and they’re associated with heavy burden of symptoms in our patients. They generally have poor prognosis, especially if diagnosed in advanced stages. And while chemotherapy is an integral part of treatment in advanced stages, additional agents can be added to therapy based on the biomarkers present. And this allows for a more personalized approach to individual patients and can lead to better outcomes. And there are multiple types of biomarkers that are used for upper GI cancers now.

Dr. Matkowskyj, can you please provide an overview of established and emerging biomarkers?

Dr. Matkowskyj:

Of course. We often talk about established biomarkers like programmed death ligand-1, or PDL-1, human epidermal growth factor receptor-2, or referred to as HER-2, microsatellite instability or mismatch repair deficiency, MSI or DMMR, have typically been well studied in clinical scientific trials and are used to inform clinical decisions.

While emerging biomarkers like CLDN 18.2 and others are currently being investigated in studies, these can help identify previously undefined subsets of patients.

These emerging biomarkers like CLDN 18.2 and others reveal more opportunities to care for patients within this disease space. Beyond gastric cancer, biomarkers have the potential to be important in several other types of cancers that include breast, lung, and colorectal cancer.

Dr. Turck:

Dr. Uboha, in this era of personalized therapies, why is biomarker testing more important than ever to help drive care, including in gastric cancer? And why should it be discussed earlier in the course of treatment?

Dr. Uboha:

Well, biomarker testing is important for the selection of an appropriate treatment plan. Knowing what biomarkers are present may help improve the prognosis and outcomes for other patients.

And we can also make sure that patients who are unlikely to benefit from a particular treatment based on the lack of a particular biomarker in their tumor are not exposed to unnecessary toxicities associated with the systemic therapies.

Dr. Turck:

And with that information in mind, Dr. Matkowskyj, would you talk a little about the typical biomarker algorithm from initial patient diagnosis throughout the course of their disease? Have there been any recent shifts in testing frequencies and patterns?

Dr. Matkowskyj:

Yes, of course. You know, this can often be institution dependent, but generally speaking, at diagnosis, most institutions will order microsatellite instability or mismatch repair testing for all patients up front. When gastric or gastroesophageal cancer is in the advanced or metastatic stages, pathologists will test for HER2 and PD-L1. For patients that have received prior HER2 targeted therapy, repeat biomarker testing tends to be performed as well.

From my perspective, it's important for physicians to provide background information on their patient and the disease state so that we know which biomarkers to order for these patients. Our goal is to work together with our oncologists to ensure that we can get timely results to inform clinical decisions for the patient, given the quick disease progression in gastric and gastroesophageal junction cancers.

Dr. Turck:

So, Dr. Matkowskyj, how has the role of established biomarkers, such as HER2 and PD-L1, influenced physician perceptions of emerging biomarkers, such as Claudin 18.2? And how prevalent is it in locally advanced unresectable/metastatic gastric and GEJ cancer?

Dr. Matkowskyj:

Great question. As I had mentioned earlier, um, given that PDL-1, HER-2, MSI or MMR are established biomarkers, they are well studied in scientific clinical trials and are used to inform clinical decisions. For example, HER-2 positivity has been reported in approximately 22% of patients, while MSI high is present in about 4%.

The HER-2 biomarker has a variety of good qualities. The biomarker is quick to perform and includes clear guidelines on the interpretation. PDL-1 can be a robust biomarker, but its heterogeneity makes it a little bit more difficult to interpret. PDL-1 is assessed using a qualitative immunohistochemical assay.

This gives us a roadmap for emerging biomarkers like CLDN 18.2 & others, and the potential a biomarker has to identify previously undefined subsets of patient populations.

Dr. Uboha, can you provide additional background on Claudin 18.2?

Dr. Uboha:

Absolutely. So CLDN 18.2, as we have said earlier, is an emerging biomarker. CLDNs are a component of tight junctions and they are involved in the regulation of permeability, barrier function, and polarity of epithelial layers.

According to recent studies, approximately 38% of locally advanced unresectable or metastatic, gastric or GE junction cancers have, um, positivity for CLDN 18.2. And CLDN 18.2 tumors were defined as having at least 75% of tumor cells with strong to moderate membranous staining intensity as determined by a validated immunohistochemistry assay.

Based on what I hear from my pathology colleagues, CLDN 18.2 appears to be a biomarker that will be fairly easy to interpret in clinical practice. The scoring depends on both membrane staining intensity, for example, moderate to strong staining, as well as percent of positive tumor cells, for example, a cut-off of 75%.

Dr. Turck:

For those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Drs. Nataliya Uboha and Kristina Matkowskyj about biomarker testing methods currently used and novel biomarkers on the horizon.

Now let's switch gears a bit, Dr. Matkowskyj, what are some groups or guidelines, that you refer to, to stay up to date on biomarkers and gastric or GEJ cancer that you would recommend? And would you also explain the importance of molecular testing?

Dr. Matkowskyj:

The National Cancer Care Network, which we refer to as the NCCN, has guidelines that support using biomarkers to help map the path forward for patients. A few examples of the guidelines include, as I had mentioned previously, testing for established biomarkers such as microsatellite instability and mismatch repair when a patient is initially diagnosed. We then ask that HER-2 and PDL-1 testing be considered in patients that have locally advanced recurrent or metastatic gastric cancer.

Molecular testing is also an important part of the diagnostic process, such as next generation sequencing, known as NGS. The markers already discussed utilize immunohistochemistry, or IHC, fluorescent insight to hybridization, or FISH. Other modalities like targeted PCR, also referred to as polymerase chain reaction, and are considered first steps. The implementation of molecular testing also has an important effect on clinical practice and patient care.

You can go to gastriccancerbiomarkers.com to learn more.

Dr. Turck:

And as we close our discussion today, would you share some tips on how pathologists and oncologists can work together on biomarker-driven personalized care for gastric and GEJ cancer patients? Dr. Uboha, let's start with you.

Dr. Uboha:

Yes, I think this is a great question. Relationships between pathologists and oncologists are very important and can vary depending on the type of setting and institution. In academic settings, we typically have specific meetings and events where relationships can foster between oncologists and pathologists.

Community practice settings may result in more challenges, because there's less interaction and less context on the disease state or biopsy that gets shared. In terms of improvement, it is important that oncologists provide pathologists with more pertinent clinical information so that pathologists have background on the stage of disease, what to test for, and reasons for testing. For example, primary treatment selection, looking at resistance mechanisms, or clinical trial enrollment.

Dr. Turck:

And, Dr. Matkowskyj, I'll give you the final word

Dr. Matkowskyj:

Definitely. I agree with your thoughts, Dr. Uboha, and how important it is that oncologists and pathologists work together to ensure that we have all the information we need for best possible outcomes for our patients.

I do want to add that institutions typically set up scenarios and guidelines that provide pathologists with a background information needed to help inform tests that need to be ordered, such as background on the patient's disease, the underlying symptoms, and other information. Our ultimate goal is to be able to partner together to help patients get the personalized medicine they need.

Dr. Turck:

These are all great points for us to continue thinking about as we come to the end of today's program. I want to thank my guests, Drs. Nataliya Uboha and Kristina Matkowskyj, for helping us better understand current and emerging biomarkers and evolving personalized medicine in gastric and GEJ cancer. It was great speaking with you both today.

Dr. Uboha:

Thank you. It was a pleasure being here.

Dr. Matkowskyj:

It's been wonderful. Thank you so much.

Announcer:

This program was brought to you by Astellas, to learn more about biomarkers that impact gastric cancer, visit gastric cancer biomarkers dot com. If you missed any part of this discussion or to find others in the series, visit reach m d dot com. This is ReachMD. Be Part of the Knowledge.