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Incorporating Data Into Practice: Late-Breaking Highlights on G/GEJ Cancers From the 2024 GI Congress

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Dr. Janjigian:
Hello, my name is Dr. Yelena Janjigian. I'm a Medical Oncologist and Chief of GI Oncology Service at Memorial Sloan Kettering Cancer Center in New York. We are concluding the ASCO GI 2024 Congress, and it's been such a pleasure to see some updates and new abstracts at this meeting. We will highlight some of the first-line upper GI abstracts.

The theme has been to look at quality of life in our patients in first-line setting. And there were at least two abstracts that we will highlight, and there's been more, looking at health-related quality of life, both with immunotherapy-based treatments and targeted agents.

So, Abstract 286 looked at health-related quality of life in first-line HER2-positive patients treated in KEYNOTE-811. As you recall, this is a phase 3 study that changed practice in first-line patients treating with pembrolizumab plus trastuzumab and chemotherapy, compared to placebo, trastuzumab, and chemotherapy. And the FDA and the EMA had approved this combination based on the progression-free survival and overall survival benefit, that's what appears to be meaningful. We're also looking at the quality of life of these patients. With addition of more chemotherapy and more immunotherapy, there was no detriment, and in fact, the quality of life was very much preserved. Our patients had done well, because of improvement in their cancer-related symptoms. The immune-related adverse events did not dramatically worsen their quality of life. And so, we looked at 12 months, both with pembrolizumab versus placebo, and the quality of life was preserved.

Shifting gears from HER2-positive to CLDN-positive population. As you recall, the Claudin inhibitors are rapidly entering the market. First in class is medication called zolbetuximab, which is a naked monoclonal antibody targeting CLDN18.2. This is an important target as it often does not overlap with HER2 or PD-L1. And so, the Abstract 372 looked at the management of nausea and vomiting following first-line with zolbetuximab and chemotherapy treated in Claudin18.2, HER2-negative metastatic gastric and gastroesophageal adenocarcinoma. This is the conglomerate of the data from the SPOTLIGHT and the GLOW study.

So, by way of background, CLDN18.2 certainly was overexpressed on preferentially on the cancer cells but also in the normal gastric epithelium, especially if it's been eroded by inflammation or dyspepsia and reflux.

And so, for patients in whom gastric primary is present or the stomach is present in place, nausea and vomiting is the rate-limiting step on a lot of these combinations strategies. Certainly, chemotherapy can cause nausea and vomiting as well. So, Abstract 372 explored the utility of different types of medications and strategy of how clinicians can mitigate these nausea, because particularly since if we cannot continue the nausea - you know, the treatment, the efficacy can be impaired.

So, SPOTLIGHT and GLOW studies are large studies, phase 3, and we have a large population of patients that we can explore. And the summary was to look at drugs like 5-HT3 inhibitors, or ondansetron and palonosetron. And also, NK1 inhibitors like aprepitant. So, what we see is that from the study is that slowing down the infusion substantially improved the quality of life and reduced the nausea and vomiting. And also, using some of these drugs prophylactically in combination with steroids, has also dramatically improved the tolerance. So, the first six to eight zolbetuximab treatments at weeks 18 and 24, you know, really are the key periods of nausea and vomiting, the patients do get used to the regimen or they tachyphylax in the way that the nausea and vomiting subsides substantially. So, these abstracts suggest that the use of prophylactic steroids and nausea medications and slowing down the infusion as a way to mitigate and improve quality of life, which clearly has been demonstrated.

So, exciting time in gastric cancer, a lot of targeted agents. And now the data is focused more on quality of life improvement, not just survival improvement, which is very important to see and we're happy to see these updates.

Thank you for your attention.

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