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ReachMD

www.reachmd.com

info@reachmd.com

(866) 423-7849

The Role of Biomarker-Driven Therapies in the Second-Line Treatment of Advanced Gastric/GEJ Cancers: What Do the Data Say?

Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Lonardi:

Hi, everybody. This is CME on ReachMD. I'm Dr. Sara Lonardi from the Veneto Institute of Oncology, and in this brief lecture, I will review the data on biomarker approach in second-line treatment and beyond in advanced gastric cancer.

For a long time, every trial we had in second-line and beyond treatment in HER2-positive gastric cancer were, unfortunately, negative. Finally, we could see some encouraging data in a phase 2 trial, the DESTINY-Gastric01, investigating an ADC, trastuzumab deruxtecan, in previously treated HER2-positive gastric cancer. This was a randomized phase 2 trial comparing trastuzumab deruxtecan with investigator choice second-line chemotherapy, and the trial was positive with an advantage not only in overall survival for trastuzumab deruxtecan, but also in progression-free survival and overall survival.

Interestingly, even if the trial was positive in the whole population, we saw that the higher was the expression of HER2, the higher was the benefit. And also, we saw that the benefit was maintained irrespective of a new test on HER2 positivity after first line and even in the patient that was not able to receive testing for HER2. That's why we believe that this was very encouraging in all HER2-positive second-line gastric treatment.

We had another phase 2 trial, single arm, and this trial was not only in the Eastern population, but even in the Western population, the DESTINY-Gastric02. And it confirmed the data from the previous trial, both in response rate, in progression-free survival, and in overall survival. To confirm those encouraging results, a phase 3 trial, the DESTINY-Gastric04, were launched and recently completed enrollment. So we should see in the next year in a randomized fashion if trastuzumab deruxtecan is better than ramucirumab and paclitaxel that is considered the standard first-line treatment.

So, clearly, in addition to efficacy, it's important also to understand which is the toxicity of a new drug. And we have to remember that the trastuzumab deruxtecan is an ADC. And so, mainly, we have a chemotherapy working, using the receptor, like, as a door to deliver the cytotoxic drug where it is more efficient. And there are some specific toxicity for this kind of drug. The most important is probably the interstitial lung disease. It is rare, but it might be severe, and so we need to be able to recognize it, to monitor, and to promptly interrupt the treatment if we have a pneumonitis grade 1, and try to treat very, very early the patient to avoid to have grade 3 and grade 4.

In addition, we also have, for this drug, nausea and vomit. It is quite frequent, and according to the NCCN Guidelines, it's important to treat like a high emetic risk with all the more effective antiemetic treatments, like olanzapine, NK1RA, 5-HT3RA, and dexamethasone.

So in the future we will have, in HER2-positive advanced gastric cancer in second-line, trastuzumab deruxtecan as probably the preferred new option. And in the HER2 negative, paclitaxel and ramucirumab remains as the preferred standard treatment, even if other

chemotherapy regimens are admitted, but they have less solid scientific evidence.

And thank you for your kind attention.

Announcer:

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