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First-Line Advanced Gastric Cancer: Best Practices for Biomarker-Directed Treatment Approaches—A Case Study

Announcer:
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Dr. Lonardi:
Hi, everybody. This is CME on ReachMD. I'm Dr. Sara Lonardi from the Veneto Institute of Oncology in Padua, Italy, and in this brief lecture, I will review with you a case of a patient of mine treated in first-line advanced gastric cancer.

So she was a woman, 51 years old. Nothing special regarding clinical history. No main comorbidities. She started with weight loss and dyspepsia, and a gastroscopy revealed a gastric adenocarcinoma G3, and on the CT scan, thickness of the stomach wall and multiple abdominal lymphadenopathies, even not locoregional, and so she was staged as stage IV.

We asked for a biomarker, and at that time we investigated microsatellite instability, having a pMMR status and HER2, adding a 3+ by mean of immunohistochemistry.

We had at the time the KEYNOTE-811 trial and she was enrolled, receiving trastuzumab, fluoropyrimidine, and platin and pembrolizumab or placebo for 6 cycles every 3 weeks. This was discovered to be the preferred option in this patient. At the time, we didn't know, but she was able to obtain a good partial response. And so after 6 cycles, we went for maintenance with the pembrolizumab or placebo plus trastuzumab and fluorouracil, as included in the protocol.

Unfortunately, just after 3 cycles of maintenance, she started having fever, hypotension, and she was admitted at the inpatient unit to understand why these kind of symptoms. And we also had tachycardia, desaturation, and we discovered a pericarditis. Immediately, we thought about the toxicity from immune checkpoint. Clearly, she was in the trial and so we didn't know at the time if she was on treatment with the pembrolizumab or placebo, but the symptoms were quite clear. And we started to treat her with the prednisolone 1 mg/kg/day, colchicine, and ibuprofen. And she very quickly recovered.

Unfortunately, at the CT scan just after recovering from this immune pericarditis, we detected a mild disease progression with an increased T stage and lymph node, but without new lesion. At the time, we had the possibility to offer them the treatment with trastuzumab deruxtecan within the DESTINY-Gastric02 trial, so we enrolled her and she received, from July 2020 to February 2021, trastuzumab deruxtecan for 11 cycles, obtaining a deep partial response.

Eventually, she progressed and we tried to find another biomarker with a comprehensive genome profiling. We didn't find any, and so we proposed one of the late-line options, paclitaxel/ramucirumab as third-line, and then even FOLFIRI as the fourth-line.

In this case of HER2-positive gastric patient, we were able to offer chemoimmunotherapy and target therapy in first line. Then in second-line, a new HER2 inhibitor, an ADC plus trastuzumab deruxtecan. And then, two chemotherapy options as third and fourth line, obtaining more than 2 years' overall survival from the starting of the first line.

My conclusion is that HER2 PD-L1 CPS and MSI are pivotal biomarkers for first-line treatment choices and also in the subsequent line. There are other biomarkers that will be important in the future.

And thank you for your kind attention.

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