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Patient Case: How Do HER2-Directed Therapies Fit Into the Biliary Tract Cancer Treatment Landscape?

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

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Dr. Pant:
This is CME on ReachMD, and I'm Dr. Shubham Pant.

Let's start our discussion by looking at a case: 56-year-old female presenting with fatigue, weight loss, and vague abdominal pain. She underwent a CT of the abdomen and pelvis, which found a 7-cm hypodense liver lesion with multiple satellite lesions adjacent to the dominant liver mass and periportal lymphadenopathy. A biopsy revealed adenocarcinoma that was consistent with the diagnosis of cholangiocarcinoma or bile duct cancer. PET scan showed a large liver mass that was hypermetabolic in addition to multiple hypermetabolic liver lesions and periportal lymph nodes. Molecular testing was performed, and it was found that the tumor was IDH and FGFR wild-type and the tumor was HER2 positive 3+ by IHC.

The patient was started frontline on gemcitabine, cisplatin, and durvalumab, which is a checkpoint inhibitor. After 6 months, patient's cancer progressed though her ECOG PS was preserved at 1. There was a serum next-gen sequencing, a ctDNA, which found the ERBB2 amplification or HER2 amplification. Now what treatment would recommend next?

The right answer for this is probably trastuzumab deruxtecan, though you could also take FOLFOX. And the reasoning is when the second-line trial was done with FOLFOX versus best supportive care, FOLFOX was better than best supportive care, but the response rate with FOLFOX was 5%, compared to trastuzumab deruxtecan in which patients with biliary tract cancers who had IHC 3+ had a high response rate of 56.1%. So though you could use FOLFOX in this case, if eligible, patient could use trastuzumab deruxtecan. The other important factor is that the patient still maintained the HER2 overamplification, which was tested just before this agent was given, and that's important.

But remember, trastuzumab deruxtecan has its own side effects. Just because it's an ADC does not mean it's not got side effects. You can look at side effects which are normally nausea, anorexia, vomiting, and hematological toxicities, but you always have to look out for interstitial lung disease also.

So though you could use chemotherapy, based on the recent approval of trastuzumab deruxtecan in HER2 IHC 3+, which is tumor agnostic, including biliary tract cancers, you might want to consider trastuzumab deruxtecan in these patients.

Now I'm going to briefly discuss the NCCN Guideline recommendations for unresectable metastatic biliary tract cancers which are HER2 amplified. And in these patients the NCCN Guidelines say that you can either go with trastuzumab and pertuzumab, and that is based on a basket trial called MyPathway, which showed a response rate of 23% in these patients with HER2-amplified biliary tract cancers. You can use trastuzumab deruxtecan which now has an approval in the setting. You can also use a combination of tucatinib with trastuzumab, and this was based on another basket trial which was presented in ASCO 2023 in which patients had a response rate of

47% with tucatinib and trastuzumab in HER2-overexpressing biliary tract cancers.

To summarize the key points of the discussion, if a patient with biliary tract cancer has HER2 3+ disease, they have multiple treatment options after frontline therapy. NCCN Guidelines do state a trastuzumab with pertuzumab, or you could use trastuzumab with tucatinib. Also, trastuzumab deruxtecan, which is an ADC, has been approved in this setting for IHC 3+ disease.

With that, my time is up. I hope this brief case review was useful to you. Thank you so much for listening.

Announcer:
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