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Understanding CNS Lesions in HER2+ Metastatic Breast Cancer

Announcer:
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Dr. Sammons:
Hello everyone. I'm Dr. Sarah Sammons, and this is CME on ReachMD. In this brief lecture, I will discuss the incidence of brain metastasis in HER2-positive breast cancer, when we might expect those brain metastasis to happen, and some risk factors for brain metastasis in HER2-positive MBC.

So, brain metastasis are something in our patients with HER2-positive MBC that are very common in the clinic. They occur somewhere between 30 and 50% of our patients that have metastatic HER2-positive breast cancer. Some risk factors for developing brain metastasis in our patients with HER2-positive MBC are actually estrogen negativity or having a HER2-enriched phenotype. Also, young age, particularly age less than 45, is a risk factor, and also having liver or lung metastasis as a site of metastatic disease is also a risk factor for our patients.

We also have data and something that we're seeing more and more in the clinic is this entity called isolated bra in relapse, meaning that the patients only relapse in the brain. So, it's not an uncommon scenario in the clinic for us to see a patient with early-stage HER2-positive breast cancer who we treated with curative intent; maybe they had a pathologic-complete response, maybe they did not. But it is not uncommon for us to actually see disease relapse in the brain only.

And the reason is that in the early-stage setting, we're mostly using monoclonal HER2-directed antibodies and TDM1, which have fairly limited brain penetration.

And so, we are actually seeing somewhere around 3% of patients with early-stage HER2-positive breast cancer have brain-only relapse, which is always very distressing to the patient. It's kind of unclear how we should treat brain-only relapse in our patients with HER2-positive MBC. However, what is generally recommended is certainly local therapy to the brain metastasis, including either surgery, without or without radiation, or radiation with or without surgery, that is. And then, we do feel very strongly that some sort of HER2-directed therapy should follow the local therapy in the setting of isolated brain relapse. And the reason for that is retrospective studies have shown that there is an overall survival benefit to giving a patient HER2-directed therapy after isolated brain relapse.

The question is, "What should we give them?" I think most of us, if a patient truly has no extracranial disease at all, and we've locally radiated most of the disease and all of the disease in their brain, then many of us will just simply choose to put the patient on trastuzumab. Certainly, the HER2CLIMB regimen could also be an option.

More studies are really needed to determine how to best treat our patients with isolated brain relapse, which is becoming an increasingly common problem. In terms of our patients that have brain metastasis that also have extracranial disease, so they also have metastatic involvement from the neck down. The treatment of those patients really depends on a couple of different factors.

The way we categorize our brain metastasis patients are really: do they have active metastasis or stable brain metastasis? Active brain metastasis are considered those brain lesions that are either untreated with local therapies like radiation, or they've been treated with radiation, but they are still progressing. Stable brain metastasis are the lesions that we have treated with local radiation, usually, and those lesions are stable or decreasing or have even gone away.

And so, we sort of think about what systemic therapies we might want to use based on those different definitions, which have been studied in clinical trials. We have two highly active agents that are active in patients with both stable and active brain metastasis. So, tucatinib, trastuzumab/capecitabine, and trastuzumab deruxtecan, or T-DXd, are both very active in stable and active brain metastasis patients. Both prolonging CNS progression-free survival and overall survival in these populations.

We do need more work and more research, and more drugs, honestly, are needed to understand how to best treat our patients who have progression after tucatinib and T-DXd, but for now, those two regimes are excellent options for our patients.

Thank you so much for your attention and thank you for watching this mini-lecture.

Announcer:
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