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State of the Union on HER2-Low Breast Cancer: Clinical Statistics & Trends

Announcer:

Welcome to *Project Oncology* on ReachMD. On this episode, sponsored by Daiichi-Sanyko, we'll hear from Dr. Pavani Chalasani, Associate Professor of Medicine at the University of Arizona Cancer Center. Dr. Chalasani joins us to discuss clinical statistics and trends in HER2-low breast cancer. Here's Dr. Chalasani now.

Dr. Chalasani:

HER2 status was thought to be fairly homogeneous in a tumor. However, recently the classifications through the American College of Pathology basically also demonstrated that there is intratumoral HER2 heterogeneity. So, when we say heterogeneity, we are implying that within the tumor, there are areas where the HER2 testing is positive, but there are also cells, or areas of tumor, where the HER2 testing is considered negative or classified as negative. That is what is defined as heterogeneity.

The HER2 heterogeneity can be found as distinct clusters of cells among which are not amplified for HER2, and they're mixed with HER2 positive or HER2 gene where HER2 is positive. So it is important to test the tumor, the entire field and figure out areas which are positive and also not as strongly positive to detect if there is intratumor heterogeneity.

The ASCO/CAP has defined the intratumor heterogeneity as areas where the HER2 FISH is positive by greater than 5 percent, but less than 50 percent of the tumor cells. So that is in one area of the definition. Or within the tumor, there was an area where the HER2 testing is negative. So that is how it is defined as to heterogeneity.

When the 2018 HER2 classification and the HER2 testing guidelines have come out, they tried to emphasize and take all the HER2 equivocal area, which were in the prior classification of HER2. When the new classification came out, and they had like five groups defined in the HER2-ish categories, to kind of help classify more as HER2 negative or HER2 positive.

And there have been a few studies since the new classification has come out in 2018, where they were trying to figure out how to reclassify the HER2 status. And there've been a few studies which have been published since then, obviously, all of them are retrospective, looking at how the HER2 equivocal cases in the prior classification would have been defined. And in a nutshell, the new classification has helped, defining, like I said, better into the HER2 positive and the HER2 negative. But in general, the HER2 positive there's a little bit, less HER2 positive cases. And they have refined in in defining it much better.

The HER2 positive breast cancers are present in about 15 to 20 percent of all breast cancer. So these are defined as HER2 3+ with complete membrane staining in more than 10 percent of cancer cells by immunohistochemistry, or where the HER2 gene, the FISH ratio is more than 2, and more than 4 gene copy number by the HER2 gene copy number. There are other classifications of HER2 positive based on the new ASCO/CAP guidelines.

However, there is a large subgroup where the HER2 immunohistochemistry is 1+ or 2+, but the FISH is negative. And they actually ended up making a majority of them. It's almost 40 to 50 percent, where the immunohistochemistry does show 1 to 2+ staining but the FISH is negative. So that's a large group. With HER2 in the immunohistochemistry is zero is about 30 to 40 percent but the low which is immunohistochemistry 1 to 2+ and FISH being negative, is a significant group of breast cancers.

However, when the HER2 is truly low, when it is immunohistochemistry 1 or 2+, but the FISH is negative, at this current time, there is no role for HER2 targeted treatments. However, in the past, there have been studies which showed that there was some signal of using HER2 targeted therapies. And now more recently, with multiple new agents coming up, which do target the HER2 protein and the gene

but especially the protein expression, there is rethinking if those tumors do respond to some kind of HER2 targeted treatments. There are antibody drug conjugates, there are bispecific antibodies, there are multiple other ways they're looking at this unique population, which, it's about almost half of all breast cancers. So the consideration is using some kind of this targeted therapies to HER2 and seeing if they would benefit and how we can use them to improve the outcomes for these patients where especially when the majority of the subgroup of HER2 is low, and majority of them do have even hormone receptor positive expression, and they're not that responsive to chemotherapy, can we take advantage of this HER2 expression to improve the outcomes, to improve responses to therapy?

There is a lot of exciting new trials coming up in that space. And again, like I mentioned before, this all comes from data from Phase 1 studies where they were looking at antibody drug conjugates and other novel agents targeting the HER2, that they did see promising responses in the HER2 low category too.

Announcer:

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