

Prognostic and Predictive Markers in Breast Cancer

The pathologist has, in modern times, acquired a more important role in the management of breast cancer. His involvement goes beyond the correct morphologic diagnosis, including grading and staging of cancer. Clinical breast oncologists make treatment decisions based on phenotypic and genotypic characteristics of the tumor, such as the presence of hormone receptors and the HER-2/neu oncogene status.

ER/PR

Estrogen and Progesterone receptor status of a primary breast tumor is not considered a major prognostic indicator, however, it is a powerful predictive marker of response to hormonal therapies and tamoxifen. ER/PR determination by immunohistochemistry remains the most reliable method to determine hormone receptor status in breast cancer. Monoclonal antibodies offer the highest level of sensitivity in detecting hormone receptors in breast cancer.

HER-2/neu

Amplification of the HER-2/neu gene and related protein overexpression are found in 10-20% of breast cancers. This gene alteration can be studied either by immunohistochemistry (IHC) looking for protein overexpression, or by fluorescence in situ hybridization (FISH) looking for gene amplification. In normal breast epithelium and in breast cancers without HER-2/neu alterations, techniques such as FISH detect two HER-2/neu signals – one on each copy of chromosome 17, and IHC shows low or absent signal representing HER-2/neu protein expression. When employing FISH technique in this setting, simultaneously looking at the HER-2/neu gene and the chromosome 17 centromeric region, the ratio of HER-2/neu to chromosome 17 signals is less than 2. In breast cancers showing HER-2/neu alterations, gene alteration is invariably present, as defined by a ratio of HER-2/neu to chromosome 17 signal of greater than 2, and IHC shows a strong membranous pattern of expression. HER-2/neu overexpression/gene amplification is an independent prognostic marker of clinical outcome in breast cancer, given the increasing role of trastuzumab (Herceptin®) in breast cancer treatment. It assists in determining which breast cancer patients would benefit from treatment with this immunotherapy directed at the HER-2/neu protein. The presence of these alteration in breast cancer can also aid in predicting positive response to doxorubicin (Adriamycin) based adjuvant chemotherapy, as well as resistance to tamoxifen, even in the setting of ER/PR expression.



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