Impact of updated HER2 testing guidelines in breast cancer - Re-evaluation of HERA trial fluorescence in situ hybridization data

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Abstract

Recently the American Society of Clinical Oncology and the College of American Pathologists have updated their clinical practice guidelines for HER2 testing in breast cancer. In order to evaluate these new recommendations, we have re-assessed the HER2 status of 6018 breast cancer cases of the screening population for the HERceptin adjuvant (HERA) trial that were originally centrally tested by fluorescence in situ hybridization based on the FDA-released test guidelines. According to the most recent 2013 ASCO/CAP recommendations, 3380 (56.2%) cases were classified as HER2 positive compared with 3359 (55.8%) applying the HERA/FDA scheme and 3339 (55.5%) applying the 2007 ASCO/CAP guidelines. Twenty-one cases switched from negative (HERA/FDA scheme) to positive (2013 ASCO/CAP guidelines). This group is characterized by a mean HER2 gene copy number of ≥6.0, polysomy or co-amplification of CEP17 with an average CEP17 count of 5, and with HER2 receptor overexpression in 75% of cases. On the basis of the HER2 gene copy number alone, we observe 494 cases (8.2%) that are in the equivocal range. Most of these cases (>80%) were also nondecisive by immunohistochemistry (score 2+) irrespective of whether ratio was . The number of equivocal cases that would require HER2 reflex testing decreases to 113 (1.9%) if in addition to the HER2 gene copy number also the ratio of HER2 and CEP17 copy numbers is considered via dual-color in situ hybridization. The combination of applying the HER2 mean gene copy number as well as the HER2/CEP17 ratio to define equivocal test decisions by fluorescence in situ hybridization as proposed by the current ASCO/CAP guidelines appears to be a more optimum approach to adopt in order to avoid or minimize reporting of false negative results. Using the mean HER2 gene copy number alone for decision making results in a significant increase of equivocal cases.

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