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SPECIFIC COMMENTS TO AUTHORS

The authors reported a case showing the disparity on IHC and FISH testing results on HER2 post neoadjuvant chemotherapy. The manuscript is well-written and easy to understand. Specific comments are: (1) The authors mentioned that only ~2% of the patients show the discrepancy on HER2 IHC and FISH testing which referred to a study by Shui R et al. Although the sample size is 12,467, it mainly represents one ethnicity. How about this phenomenon (discrepancy on IHC and FISH) in other populations around the world? (2) Luminal A breast cancer is ER and/or PR positive , HER2 negative and low Ki-67 level. Is Ki-67 level tested along with ER, PR and HER2 pre- and post-NACT? (3) The magnification of FISH figures should be indicated in the figure legend. It is preferred to use arrows to point out positive foci representing HER2 amplification. (4) Is lumpectomy a better medical term to describe "breast-conserving surgery"? (5) Is there any follow-up testing for this case? What's your opinions on the possible, post-NACT changes of the HER2 signature over time?

REPLY:

(1) Only 2% gene amplified in the negative (0/1+-)expression cases by FISH among Chinese patients in the study by Shui R while approximately 4% in other populations.

(2) Ki-67 was 20% before surgery and dropped to 2% after surgery.

(3) The magnification of FISH figures has been indicated in the figure legend. And arrows have been used to point out positive foci representing HER2 amplification.

(4) Lumpectomy has been used to describe "breast-conserving surgery".

(5) Follow-up including breast ultrasound,abdominal ultrasound and chest computed tomography were regularly monitored every 3 mo without evidence of recurrence.

Nowadays, the status of HER2 can be influenced easier due to the combination of neoadjuvant chemotherapy and HER2-targeted therapy. Therefore, verification

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procedures should be routinely performed pre- and post-NACT. The decision whether or not to administer HER2-targeted therapy or endocrine therapy is largely based on the result. And the estimation of rates of recurrence and outcome can be affected as well. We expect the patient in this report benefit from the use of Trastuzumab and Pertuzumab in the days to come.