Chromosome 17 Polysomy without HER2 Amplification Does Not Predict Response to Lapatinib in Metastatic Breast Cancer—Letter

Cathy B. Moelans, Roel A. de Weger, and Paul J. van Diest

We have read with great interest the article by Downey et al. on chromosome 17 polysomy without HER2 amplification and prediction of response of metastatic breast cancer patients to lapatinib (1). The authors report that in a group of 405 HER2 FISH-negative patients, patients with chromosome 17 polysomy (n = 44, Chr17 ≥ 2.2 or 2.0) did not show a significant benefit from HER2-directed therapy compared with nonpolysomic patients. The authors used the current definition of chromosome 17 polysomy accepted by the Food and Drug Administration and American Society of Clinical Oncology/College of American Pathologists. They comment that it is unclear if chromosome 17 polysomy increases HER2 mRNA and protein product. The authors did, however, not mention the recent observation that chromosome 17 polysomy is far less common in breast cancer than previously suggested (2–4) and may, in fact, be very rare. These 3 independent studies using comparative genomic hybridization, FISH, and multiplex ligation-dependent probe amplification report that chromosome 17 genes show complex patterns of gains and losses unrelated to the copy number status of the centromere (CEP17). This could be another explanation for the fact that the study of Downey et al. could not confirm an association between “polysomy 17” and an improved outcome with the addition of lapatinib to paclitaxel, previously observed by Kaufman et al. (5).

The conflicting results of Downey et al. and Kaufman et al., but also the recent study by Bartlett et al. (6), indicate that large prospective clinical trials are necessary to validate whether patients showing increased CEP17 indeed show a better response to HER2-targeted therapies and anthracyclines, also in the absence of HER2 or topoisomerase 2 (TOP2A) amplification. In addition, these studies should assess chromosome 17 status in a less simplistic way than merely looking at CEP17 and HER2 gene copy number, to help elucidate the mechanism by which CEP17 or other pericentromeric chromosome 17 genes could possibly influence trastuzumab/lapatinib and anthracycline sensitivity.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Received 03/26/2010; revised 05/06/2010; accepted 05/28/2010; published online 12/15/2010.

References

Chromosome 17 Polysomy without HER2 Amplification Does Not Predict Response to Lapatinib in Metastatic Breast Cancer—Letter

Cathy B. Moelans, Roel A. de Weger and Paul J. van Diest

Clin Cancer Res 2010;16:6177.