BJC

British Journal of Cancer (2017) 116, e11 | doi: 10.1038/bjc.2017.61

Reply to 'Comment on 'Nomogram to predict pathologic complete response in HER2-positive breast cancer treated with neoadjuvant systemic therapy''

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Sir,

We thank K Altundag for the interest in our article (Fujii *et al*, 2017) and thoughtful comments. Kurozumi *et al* (2015) reported that Ki67 level and histological grade were significantly associated with pathological complete response (pCR) after neoadjuvant chemotherapy with trastuzumab in patients with HER2-positive breast cancer.

Polley *et al* (2013) reported that interlaboratory reproducibility of Ki67 was moderate. Although central staining demonstrated a better intraclass correlation coefficient: 0.71 (95% confidence interval, 0.47–0.78), in the setting of local staining, the intraclass correlation coefficient was low: 0.59 (95% confidence interval, 0.37–0.68). Also, the Ki67 value in patients who undergo neoadjuvant chemotherapy without endocrine therapy is still not obvious (Dowsett *et al*, 2011), and the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (https://www.nccn.org/professionals/physician_gls/f_guidelines.asp) do not recommend testing Ki67 routinely. Because of its low reproducibility and lack of recommendation as a standard of care, Ki67 staining is not routinely performed as standard practice. Therefore, we excluded Ki67 from our analysis to make our nomogram practical.

For histological grade, the hazard ratio was not significantly associated with pCR in multivariate analysis, despite the histological grade being a significant variable in univariate analysis in the study by Kurozumi *et al* (2015). Therefore, we assume that the effect of not including nuclear or histological grade in our analysis was minimal.

On the basis of these previous publications, many patients in our data set did not have Ki67 and histological grade. We agree with you that we cannot conclude anything about the clinical importance of Ki67 and histological grade in the context of neoadjuvant chemotherapy in patients with HER2-positive primary breast cancer unless we assess them in our model because this is a retrospective study.

In conclusion, the effect of not including Ki67 and histological grade in our analysis is small, but we cannot make a definite conclusion unless we perform the same analysis including Ki67 and histological grade.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Published online 14 March 2017