Discordance in Immunohistochemical Status of Breast Cancer Post Neoadjuvant Chemotherapy

Sanjit Kumar Agrawal¹ · Sanjoy Chatterjee² · Indu Arun³ · Rosina Ahmed⁴

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Dear Sir,

We read with interest the article by Anand et al. [1], Discordance of estrogen and progesterone receptors after neoadjuvant chemotherapy in breast cancer: an Indian study, recently published in the Indian Journal of Surgical Oncology (September 2016, 7 (3): 316–319 DOI [10.1007/s13193-016-0515-3](https://doi.org/10.1007/s13193-016-0515-3)). The authors retrospectively evaluated the changes in estrogen (ER) and progesterone receptor (PR) immunohistochemistry (IHC), measured before and after neoadjuvant chemotherapy (NACT) for breast cancer, and also analysed the relationship between hormone receptor expression and tumour response to primary systemic chemotherapy. We have recently published two articles with higher patient numbers [2, 3] and quality assured techniques. The first article addressed the discordance in receptor status before and after NACT and analysed the changes with respect to the outcome and factors, which predict response to primary systemic chemotherapy. We reported a significant reduction in the expression of ER ($p = 0.03$) and Ki-67 index ($p = 0.002$) following NACT, but no significant change in PR ($p = 0.82$) or HER2 ($p = 0.26$) expression. With a short median follow-up of 16 months, a change in the hormonal status from positive to negative was associated with a better RFS than a change from negative to

positive (HR = 0.24, CI 0.18–1.09, $p = 0.06$). This data is supported by the results from other centres. Van de Ven et al. [4] found that NACT-associated ER discordance varied between 2.5 and 17% and PR discordance between 5.9 and 51.7%. In a study from MD Anderson [5], the subtyping of breast cancer changed in 41% of patients if receptor status was repeated. In this study, both overall survival and relapse-free survival at 5 years were significantly better in ER-positive patients who had at least a 20% change in ER expression, compared with those where the change was of a smaller magnitude.

The author's inclusion or exclusion criteria is not clear about how many patients have completed all cycles of chemotherapy before surgery. We note that the pCR rate reported in this study is on the lower side (11.5%), versus 23% as reported in our study, and this may represent a difference in the treatment regimen as all of our patients completed their planned chemotherapy before surgery in our study. In the subgroup of patients with ER/PR negativity, the authors report a high pCR. Whilst this is more or less established, it will be interesting for readers to note that in our study [3], PR negativity was a predictor for pCR (OR 3.2, 95% CI = 1.6–6.04, $p = 0.001$), and PR positivity was associated with an improved relapse-free survival (Kaplan-Meier $p = 0.02$, Cox regression HR = 0.3, $p < 0.01$).

A growing number of studies report discordance in breast cancer IHC status related to systemic chemotherapy, but the reason for discordance is still unclear, and may be related to tumour heterogeneity [6], clonal selection [7], genetic switch [8] or differential treatment response. Our study [2] showed that pre-NACT ER/PR values were better related to outcome than post-NACT values, but it is unclear how this information should be used in the clinical setting. The authors are invited to encourage a national pathology QA program, currently under discussion in the National Cancer Grid. Such collaborative

✉ Sanjit Kumar Agrawal
sanjitgrwl@gmail.com

¹ Department of Breast Oncosurgery, Tata Medical Center, Kolkata, India

² Department of Clinical Oncology, Tata Medical Center, Kolkata, India

³ Department of Pathology, Tata Medical Center, Kolkata, India

⁴ Department of Breast Oncosurgery, Tata Medical Center, Kolkata, India

projects could allow further bigger projects that could cast further light on the important issues highlighted in this article.

Compliance with Ethical Standards

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Conflict of Interest The authors declare that they have no conflict of interest.

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