Predictors of response to neoadjuvant chemotherapy: Importance of breast cancer subtypes

Sir,

Preoperative systemic therapy in locally advanced breast cancer (LABC) has many benefits and has become widely used in the present times. The study by Bansal *et al*.[1] was a welcome addition to our knowledge. A wide range of factors predicting response to neoadjuvant chemotherapy (NACT) in LABC have been identified, but the quest remains inconclusive. In this regard, we would like to emphasize some important aspects.

Breast carcinoma as an entity is comprised of molecularly distinct diseases. It is natural that these entities would have different predictors of resistance to chemotherapy. A recently published study, de Ronde *et al*.[2] analyzed this and found that for human epidermal receptor (HER) +ve, estrogen receptor − ve breast cancer, subtype specific predictor based on clinical features outperformed the generic, nonspecific predictor. They advocated that both specific and generic predictors should be evaluated when attempting to predict treatment response in breast cancer. It primarily would depend on the specific type of predictor being evaluated.

The molecular predictors evaluated by Bansal *et al*.[1] that is, carcinoembryonic antigen related cell adhesion molecules, carcinoembryonic antigen-related cell adhesion molecule 5, 6 (CEACAM 5, 6) and SLC7A5 have been used as predictors of therapy in breast cancer earlier. CEACAM 6 has also been used to predict breast cancer recurrence to endocrine therapy. In a study, Maraqa *et al*.[3] retrospectively tested whether significantly up-regulated CEACAM 6 on immunohistochemistry specimens was predictive of breast cancer resistance to tamoxifen therapy on long term follow-up. The results were indicative of significantly more CEACAM 6 expression in the relapsed group of patients as compared to nonrelapsed control, supporting an important role of CEACAM 6 in endocrine resistant breast cancers. Similarly, SLC7A5 has also been implicated in endocrine resistance in breast cancers. Mihály *et al*.[4] in a meta-analysis to validate predictors to tamoxifen resistance identified SLC7A5 as one of the most promising genes along with two other genes.

Tsang *et al*.[5] evaluated CEACAM 6 expression in two independent cohorts of invasive breast cancer patients, and CEACAM 6 expression was found in 37.1% of invasive cancers. It was significantly positively correlated with HER two expression especially the HER overexpressed subtype. In this subtype, it was associated with high nodal stage patient outcome.

Thus, it needs to be prioritized that expression of these three molecular predictors be correlated with receptor/molecular subtypes of breast cancer to know their exact significance as a predictor of response to neoadjuvant therapy in carcinoma breast. It would have been highly appreciable to know the correlations of the molecular markers with breast cancer subtypes in the study done by Bansal *et al*.[1] The molecular markers CEACAM 6 and SLC7A5 have been proven as markers of endocrine

resistance in various studies and need to be studied in that context.

To sum up, there is a dire need of clinically evaluable markers of response to NACT, and if markers such as CEACAM 6 and SLC7A5 are evaluated in the right perspective, they may help to fill the gap.

Mukesh Sharma, Swaroop Revannasiddaiah[1], Muninder Negi[2], Ratti Ram Negi[2]

Department of Radiotherapy, Regional Cancer Centre, Indira Gandhi Medical College, Shimla, [2]Department of Radiotherapy, Dr. Rajendra Prasad Government Medical College, Tanda, Kangra, Himachal Pradesh, [1]Department of Radiation Oncology, Swami Rama Cancer Hospital and Research Institute, Government Medical College, Haldwani, Nainital, Uttarakhand, India

Correspondence to: Dr. Mukesh Sharma, Department of Radiotherapy, Regional Cancer Centre, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India.
E-mail: muk00008@gmail.com

REFERENCES

1. Bansal A, Garg M, Chintamani C, Saxena S. Immunohistochemical expression of carcinoembryonic antigen-related cell adhesion molecules 5, CEACAM6, and SLC7A5: Do they aid in predicting the response to neo-adjuvant chemotherapy in locally advanced breast cancer? Clin Cancer Invest J 2014;3:521-5.
2. de Ronde JJ, Bonder MJ, Lips EH, Rodenhuis S, Wessels LF. Breast cancer subtype specific classifiers of response to neoadjuvant chemotherapy do not outperform classifiers trained on all subtypes. PLoS One 2014;9:e88551.
3. Maraqa L, Cummings M, Peter MB, Shaaban AM, Horgan K, Hanby AM, *et al.* Carcinoembryonic antigen cell adhesion molecule 6 predicts breast cancer recurrence following adjuvant tamoxifen. Clin Cancer Res 2008;14:405-11.
4. Mihály Z, Kormos M, Lánczky A, Dank M, Budczies J, Szász MA, *et al.* A meta-analysis of gene expression-based biomarkers predicting outcome after tamoxifen treatment in breast cancer. Breast Cancer Res Treat 2013;140:219-32.
5. Tsang JY, Kwok YK, Chan KW, Ni YB, Chow WN, Lau KF, *et al.* Expression and clinical significance of carcinoembryonic antigen-related cell adhesion molecule 6 in breast cancers. Breast Cancer Res Treat 2013;142:311-22.

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.148983