Editorial

Robust Guidelines for the Management of HR+ Her2− EBC: Crucial Value of CanAssist Breast

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We congratulate Parikh et al for putting together this guideline for HR+ Her2− early breast cancer (EBC).[1] As we gather this is a culmination of 2 years work that is bold as well as robust enough to give the correct, unambiguous, and clearcut guidance to the community oncologists.

They have followed a step-by-step process (modified Delphi) that is both transparent and fair.[2]

Most authors focus on numbers. In the development of guidelines, they sometimes forget that the document will finally be used by the community oncologists who otherwise may not have access to the expertise and mentorship of a senior experienced colleague. While focusing on increasing numbers, many previous publications have lost sight of the rigor required or the level of expertise necessary to be mature enough to guide others in tier two or three cities.[3]

Where breast cancer is concerned, more than any other cancer, the value of a multidisciplinary team cannot be underestimated.[4] Parikh et al took the right first step by conducting a survey including 185 oncologists, of which 65% were senior medical oncologists. This adds to the robustness of the entire methodology used and we appreciate the same.

Parikh et al used a well-established, predefined systematic method (modified Delphi). We have used the same process earlier, published our recommendations, and have received positive feedback regarding their utility.[2] Such guidelines are simple to implement by the community oncologists and the process helps give confidence in the patient party.

In the current age of personalized medicine and precision oncology, our focus is to offer the appropriate treatment to those who will benefit most from it and avoid giving it to those where risk outweighs the potential benefit. It is well established that patients with EBC having a low risk of recurrence do not benefit from chemotherapy. In the past, we have found it difficult to achieve this consistently because the only available tests were those discovered and validated in the Caucasian population of United States and Western Europe.[5,6] Only a miniscule, if any, patients from India have been included in this or similar Western trials. And we all know that blind application of such markers or scorings in the Indian population is not only inappropriate but can also lead to wrong treatment of patients.[5,6]

Fortunately, CanAssist Breast is the test that has been prospectively validated in our context; data of this phase 3 trial was presented at ESMO Breast in May 2022.[7]

There is ample evidence that such biomarkers, like CanAssist Breast, need to be given priority when arriving at the treatment plan for individual patients, more so than clinical

parameters.[8,9] In other words, when clinical parameters indicate high risk but biomarker score is in favor of low risk, it is safe to avoid additional unnecessary treatment.

In today's era of next-generation sequencing (NGS), gene-based prognostic and predictive testing is increasingly advocated. However, they have not been able to displace age old protein-based biomarker testing like hormone receptor testing by immunohistochemistry (IHC). This is because these tests have become objective and are time tested over generations. In fact, the more modern NGS tools with higher sensitivity often throw up false negative results or bring to light mutations of unclear significance—the so-called variance of undetermined significance. To this we can add the complexity of the NGS data analytics. While India may have 600 NGS machines among its various laboratories, the turnaround time continues to remain 4 to 6 weeks because of the bioinformatics bottleneck. No wonder, even when the same genetic change can be identified with various techniques, IHC still remains the gold standard, as with ALK (anaplastic lymphoma kinase) mutations seen in lung cancer.[10]

With CanAssist Breast having completed 6 years of real-world clinical utility in India, we look forward to it guiding the treatment decisions among more and more patients with HR+ Her2− EBC, avoiding unnecessary toxicity among low-risk category and ensuring systemic therapy preventing recurrence in the high-risk category.

Conflict of Interest
None declared.

References

1 Parikh PM, Bhattacharyya GS, Biswas G, et al. Practical consensus recommendations for optimizing risk versus benefit of chemotherapy in patients with HR positive Her2 negative early breast cancer in India. South Asian J Cancer 2021;10(04):213–219

2 Thirumalairaj R, Parikh PM, Agarwal A, et al. South Asian Declaration-Consensus Guidelines for COVID-19 vaccination in cancer patients. South Asian J Cancer 2021;10(01):3–8

3 Doval DC, Kumar P, Talwar V, et al. Shared decision-making and medicolegal aspects: delivering high-quality cancer care in India. Indian J Palliat Care 2020;26(04):405–410

4 Doval DC, Radhakrishna S, Tripathi R, et al. A multi-institutional real world data study from India of 3453 non-metastatic breast cancer patients undergoing upfront surgery. Sci Rep 2020;10(01): 5886. Doi: 10.1038/s41598-020-62618-3

5 Albain KS, Gray RJ, Makower DF, et al. Race, ethnicity and clinical outcomes in hormone receptor-positive, HER2-negative, node-negative breast cancer in the randomized TAILORx trial. J Natl Cancer Inst 2021;113(04):390–399

6 Batra A, Patel A, Gupta VG, et al. Oncotype DX: where does it stand in India? J Glob Oncol 2019;5:1–2

7 Xi Z, Gunda A, Kranenbarg EMK, et al. 9P-Long term recurrence risk predictions by CanAssist Breast in a sub-cohort of TEAM. Poster presented at ESMO Breast. Berlin, Germany; 2022

8 Bakre MM, Ramkumar C, Attuluri AK, et al. Clinical validation of an immunohistochemistry-based CanAssist-Breast test for distant recurrence prediction in hormone receptor-positive breast cancer patients. Cancer Med 2019;8(04):1755–1764

9 Ramkumar C, Buturovic L, Malpani S, et al. Development of a novel proteomic risk-classifier for prognostication of patients with early-stage hormone receptor-positive breast cancer. Biomark Insights 2018;13:1177271918789100

10 Batra U, Nathany S, Sharma M, et al. IHC versus FISH versus NGS to detect ALK gene rearrangement in NSCLC: all questions answered? J Clin Pathol 2022;75(06):405–409