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Molecular characterization of Breast cancer: Clinical implication on patient's management

Shahla Masood
University of Florida, USA

As a major public health problem, breast cancer remains a second leading cause of cancer death among women across the globe. Breast cancer is not only a physical disease with significant mortality and morbidity, but it is also associated with remarkable psychosexual impairment. The significance of the impact of breast cancer on women's lives has resulted in an international effort to fight against this disease. Recent decline in mortality from breast cancer in resource-rich countries is attributed to increased public awareness, advances in breast imaging and screening and to the new innovations in breast cancer therapy. The new discoveries about the biology of this disease and the introduction of molecular targeted therapy are exciting and may potentially further reduce mortality from breast cancer. The challenge, however, is the heterogeneity of breast cancer in presentation, clinical behavior and response to therapy. It is clear that there is a critical need for the delivery of personalized medicine for breast cancer patients. Planning individualized therapy for each breast cancer requires access to effective tools for appropriate stratification of patients. It is important to identify those who may require aggressive therapy versus those who may not need or may not respond to similar therapy. Traditional clinical and pathologic factors such as age, histologic grade, tumor type, tumor size, and hormone receptors are commonly used to assign patients into risk groups to receive adjuvant hormonal, radiation therapy and/or chemotherapy. These factors accurately stratify the patients based on the long term follow up studies. However, it is recognized that traditional prognostic factors are limited in their ability to provide reliable stratification in all patients. It has been shown that up to 30% of women with node negative breast cancer die of the disease regardless of adjuvant therapy, and 70% survive without adjuvant therapy. In addition, heterogeneity in breast cancer can not be captured by the traditional prognostic factors. Therefore it is essential to search for factors that may supplement traditional prognostic factors in segregating patients who need adjuvant therapy and in predicting clinical response to the available therapeutic modalities. There is also a need to develop additional forms of systemic therapy for those tumors that fail to express known targets such as estrogen and progesterone hormone receptors and HER-2/neu oncogenes. Breast cancers are diverse in their natural history and their responsiveness to treatment. Differences in transcriptional programs account for much of the biological diversity of breast tumors. In each cell, signal transduction and regulatory systems transduce information from the cell's identity to its environmental status that controls the level of expression of every gene in the genome. It is proposed that phenotypic diversity of breast tumors might be accompanied by a corresponding diversity in gene expression patterns that can be captured using cDNA microarrays. It is assumed that the expression of various genes in different tumors provides an opportunity to classify tumors at a genomic level into subclasses of potential prognostic significance.

Allogeneic stem cells transplantation for chronic myeloid leukemia in the era of tyrosine kinase inhibitors: What are the limitations?

Sehar Afreen and Zakariya Al Safran
King Fahad Specialist Hospital, Kingdom of Saudi Arabia

The treatment strategies for chronic myeloid leukemia have changed dramatically with the advent of tyrosine kinase inhibitors. Since they provide excellent opportunity for complete cytogenetic and molecular remissions, they are recommended as a first line therapy. Yet their discontinuation always leads to disease relapse. Allogeneic stem cell transplantation remains the only cure at present. However, several factors affect the safety and efficacy of this approach. Combination strategies involving allogeneic hematopoietic stem cells transplant and tyrosine kinase inhibitors are also under investigation. This review highlights their major limitations and the areas of studies required improving the clinical outcomes.

seharafreen@yahoo.com