Selected Summary

HER2 Status and Efficacy of Adjuvant Anthracyclines in Early Breast Cancer: a Pooled Analysis of Randomized Trials.

Gennari A, Sormani MP, Pronzato P, Puntoni M, Colozza M, Pfeffer U, Bruzzi P. J Natl Cancer Inst. 2008 Jan 2; 100(1):2-4.

INTRODUCTION

Over the past decade great strides have been achieved in the treatment of breast cancer. Molecular markers like amplification of Human Epidermal Growth Factor (HER2), not only help in prognosticating patients but are also defining various subgroups of patients with different response to chemotherapy regimes.[2, 3]

Anthracycline containing regimes are currently the standard of care in early breast cancer.[2] Various studies have shown that HER2 status is a positive predictive marker for response to anthracycline based regimes. These studies individually are weak in demonstrating the above effects. The meta-analysis of 8 such studies conducted by Gennari et al[1] not only strengthens the above observations but also provides the clinician with a valuable tool for improving survival chances in patients while minimizing side effects.

SUMMARY

Gennari et al identified 8 studies which compared anthracycline based with non anthracycline based adjuvant chemotherapy regimes in the treatment of early breast cancer and their association with HER2 status. The 8 studies had altogether 6564 randomly assigned patients. Information on HER2 status was available for 5354 patients, of which 1536 patients were positive for HER2. Statistical analysis was done by inverse variance weightaghe to calculate log hazard ratios (HRs) for disease free and overall survival according to HER2 status. Data on disease free survival was available from 6 studies and overall survival from 7 studies. The results of the meta-analysis showed that in HER2 positive disease (n= 1536 patients), anthracycline were superior to non anthracycline based regimes in disease free survival and overall survival. The pooled hazard ratio (HR) for the risk for relapse was 0.71 (P< .001), and the HR for the risk for death from any cause was .73 (P< .001). Women who were HER2 negative did not show any benefit in disease free or overall survival with anthracycline based regimes. The pooled HRs for the risk for relapse was 1 (P = .75) and risk for death 1.03 (P= .60). The authors concluded from the above meta-analysis that the use of anthracycline in the adjuvant treatment of HER2 negative patients is no longer justified. The beneficial effect of HER2 status on response to anthracycline based chemotherapy was independent of the type of anthracycline used, proportion of patients assayed for HER2 status and the type of assay used.

COMMENTS:

Gennari et al[1] have conducted a landmark meta-analysis. Their study has opened up an active debate on treating patients according to their tumour molecular profile. The meta-analysis looked at all the available studies and has thoroughly analyzed them to extract the relevant results and avoid any bias. Anthracyclines are

associated with significant cardiac toxicity.[4] Defining which patients would benefit maximum from anthracycline would help in avoiding unnecessarily treating patients with these drugs and thus minimizing cardiac toxicity and subsequent morbidity. But does the study provide us with conclusive answers for formulating new recommendations? Looking at the results of 2 recently conducted trials given below;[5-6] we have a long way to go before we find the right combination of chemotherapy regime tailored to a given molecular profile. Recently the Breast Cancer International Research Group 006 trial has shown that clinical outcome of non anthracycline based regimes to be equal to anthracycline based regimes when combined with Trastuzumab in HER2 positive patients.[5] But the US oncology Group study has also showed the above results without selecting for HER2 status.[6] Combination of trastuzumab and anthracyclines are additive for cardiac toxicity.[7] Thus, it's more important to find equally efficacious non anthracycline based regimes for treatment of HER2 positive breast cancer. The study by Gennari et al has opened a Pandora's Box. It would be too premature to abandon time tested anthracycline based regimes for HER2 negative cancers. It would be prudent to wait for the results of ongoing research before arriving at any conclusion.

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