ANTHRA IN ADJUVANT SETTING FOR

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LUMINAL A TYPE OF EARLY BREAST CANCER

‘Luminal A-like’

ER-positive
HER2-negative
Ki67 low
PgR highb
‘

Low-risk molecular signature (if available)

INDICATION OF CHEMO

- ET should be used in all luminal-like cancers [I, A]. Indications for ChT within this subtype depend on the individual's risk of re- lapse, taking into account the tumour burden and features suggestive of biological aggressiveness (grade, proliferation, vascular invasion), presumed responsiveness to ET and patient preferences [I, A]. Features associated with lower endocrine responsive- ness include low steroid receptor expression, lack of PgR expression, high tumour grade and high expression of proliferation markers.

HIGH RISK ?

- For those with luminal-A like tumors, only those EBCs with high tumor burden (>4 lymph nodes, T3 or higher) should be considered for chemotherapy, as endocrine therapy alone is usually sufficient in most cases.

- Anthracyclines have been the backbone of adjuvant chemotherapy for breast cancer in the last 30 years.

- Any chemo drug combination used for more than 30 years?

WAY BACK IMPORTANCE OF ANTHRACYCLINES

- Later trials showed that substitution of methotrexate with epirubicin (CEF) was even more efficacious both in terms of DFS and OS in premenopausal women with axillary node-positive breast cancer [18]. The advantage of anthracycline-containing 3-drug combinations over CMF was unequivocally confirmed in an individual-patient data meta-analysis of the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) [1]. Altogether, 100,000 patients in 123 randomized trials were included. Anthracycline-based regimens with substantially higher cumulative dosage than standard 4 × AC (adriamycin and cyclophosphamide) (e.g. CAF (cyclophosphamide, adriamycin, and fluorouracil) or CEF) were superior to standard CMF (response rate (RR) 0.78; p = 0.0004).
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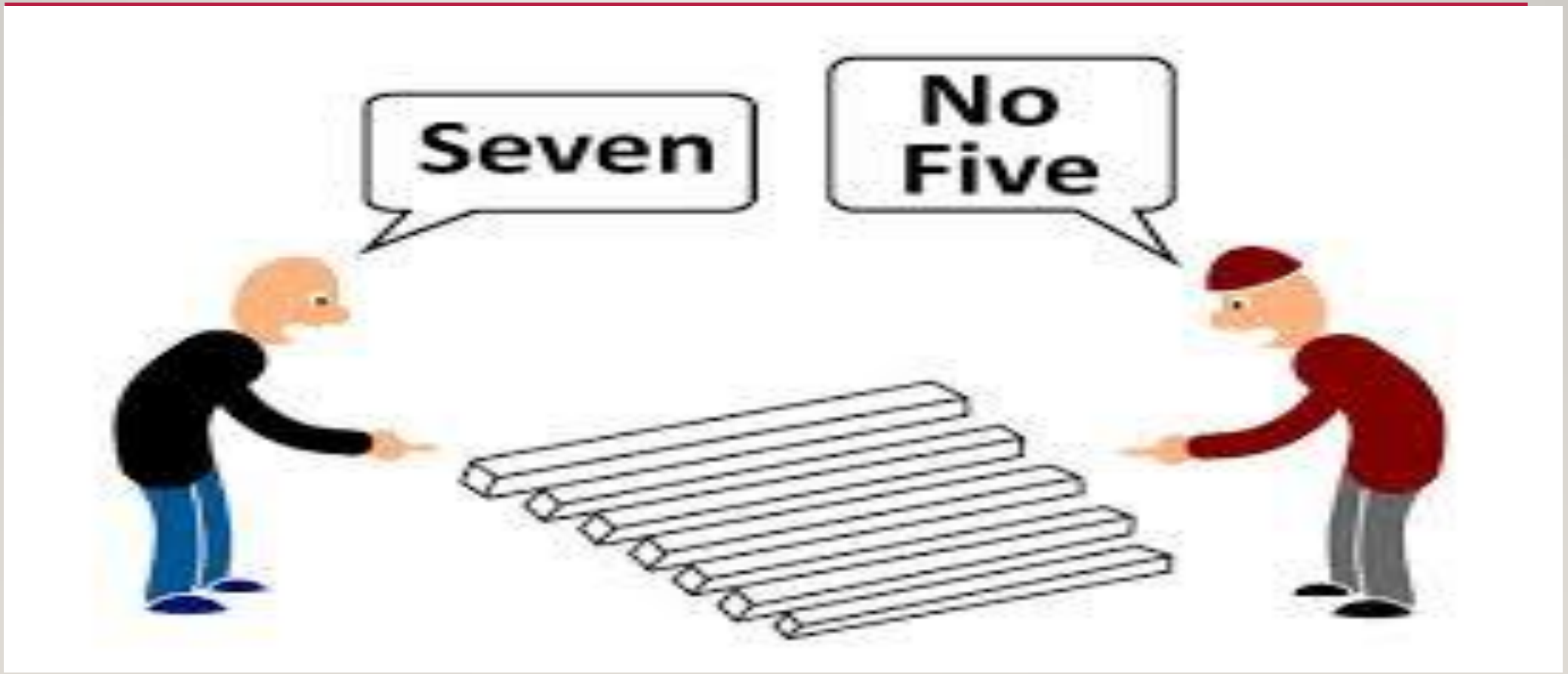
- Most adjuvant chemotherapy trials were performed in unselected patient populations or, more precisely, in populations selected according exclusively to anatomy (axillary status) or demographics (menopausal status) rather than tumor biology. Most of these trials did not stratify patients according to hormonal status, even though the relevance of this biologic factor was well known at the time when the trials were designed.

- We know that, overall, the taxane containing combinations are superior to anthracycline (nontaxane) containing combinations, and that the anthracyclines performed better than CMF.
- In general, however, this superiority is associated with more toxicity. Furthermore, the benefit of the newer combinations over the older ones is small (3% to 5% in absolute terms),

we cannot identify the subsets of patients who actually benefit from the new drugs. In other words, we need to treat 100 patients to benefit only three to five of them, while administering what is usually a more toxic treatment to the remaining 95 to 98 patients who do not derive any survival benefit.

- **Anthracycline-Based Chemotherapy vs Docetaxel/Capecitabine: What's the Better Adjuvant Therapy for Early Breast Cancer?**
- phase III EORTC 10041/BIG 3-04 MINDACT trial, though underpowered, suggested no benefit of docetaxel/capecitabine vs standard anthracycline-based adjuvant therapy for patients with early breast cancer at high clinical risk and/or high genomic risk.

CONTROVERSY POINT



Anthracycline versus nonanthracycline adjuvant therapy for early breast cancer

A systematic review and meta-analysis

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BREAST CANCER: AN OVERVIEW OF PUBLISHED INDIAN DATA

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- There has been a considerable concern regarding the toxicity of chemotherapy in Indian women and this has been addressed in many trials.
- The rate of cardiac toxicity is reported to be <2%.
- In the trials that evaluated taxanes, the incidence of hypersensitivity reactions to paclitaxel is approximately 5%.

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ADJUVANT CHEMOTHERAPY IN BREAST CANCER: TO USE OR NOT TO USE, THE ANTHRACYCLINES

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- We personally believe that the anthracyclines still have an important role in the (neo)adjuvant care of patients with early stage breast cancer. Anthracyclines plus taxanes are important components of what is called today "third generation regimens"[13]. These include regimens such as 3 cycles of CEF followed by 3 cycles of docetaxel (CEF-D) as developed in the PACS 01 trial[54]; 4 cycles of AC followed by paclitaxel or docetaxel as used in the CALGB 9741 and ECOG 1199 clinical trials[55,56], 6 cycles of doxorubicin, cyclophosphamide and docetaxel (TAC) as in the BCIRG 001 trial[57] and the trastuzumab containing regimens from the NCCTG 9831, NSABP B-31 and BCIRG 006 studies previously discussed[44,45].

CONCLUSION

- Despite failing to show noninferior to the non-A in patients with EBC, it provided evidence that both regimens significantly improved the DFS and OS, and TC regimen may be noninferior to anthracycline-contained regimens.


For good ideas and true innovation, you need human interaction, conflict, argument, debate.
Margaret Heffernan
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