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Title:

Her 2 and Response to Paclitaxel in Node Positive Breast Cancer

Background:

- Previous literature suggests that Her2 status may predict response to anthracyclines
- CALGB 9344 evaluated escalating doses of anthracyclines and the addition of paclitaxel in the adjuvant treatment of early breast cancer. Results indicated that escalating the dose of anthracycline did not lead to a improvement in outcomes, but the addition of four cycles of paclitaxel did improve DFS and OS.
- Her2 is overexpressed or amplified or both in about 15-20% of breast cancers.
- Given the significant toxicity associated with adjuvant chemotherapy, we need better biomarkers and predictors to help predict the benefit from chemotherapy.
- The authors hypothesized that Her2 status may predict response to escalating doses of anthracyclines, the addition of paclitaxel or both and evaluated the patients enrolled in the CALGB 9344 to evaluate this hypothesis.

Study design:

- CALGB 9344 enrolled 3121 patients
 - Patients had node positive breast cancer and had completed surgery with negative margins and were fit enough to receive adjuvant chemotherapy
- A random sample of 1500 women was identified from the women who participated in the CALGB 9344 study.
 - Adequate tissue specimen was available in 1,322 patient

Study results:

- The random sample was similar to the whole study sample
- There was no significant association between Her2 status and escalating doses of anthracyclines
- There was however an interaction between her2 positivity and the addition of paclitaxel
 - Hazard ratio of recurrence HR – 0.59 (p=0.01)
 - An effect that was independent of ER status
- No benefit of addition of paclitaxel was seen in patients with Her-2 negative, ER positive patients

Conclusions:



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- A significant interaction was seen between Her2 status of tumor and the addition of paclitaxel.
- There was no added benefit of paclitaxel in patients who were Her2 negative and ER positive.

Study commentary:

- Patients were randomly selected from the whole study population
- The tumor samples were only available in 1322 out of the 1500 patients. No reasons were provided by the authors as to why only selected specimens were available.

Bottomline for Canadian medical oncologists:

- AC followed by 3weekly Paclitaxel used to be a standard adjuvant chemotherapy regimen for node +ve breast cancer.
- Over the last few years there have been at least three trials that have shown superiority of other adjuvant regimens – dose dense AC followed by Paclitaxel (CALGB 9741), CEF for 6 cycles or dose dense EC followed by Paclitaxel (MA.21) and AC for four cycles followed by either weekly Paclitaxel or q 3weekly Docetaxel (E 1199).
- Hence the application of this data to current practice is limited as AC followed by 3weekly Paclitaxel is now seldom used.
- Given that adjuvant trastuzumab has clearly shown a benefit for Her2 positive early breast cancer, an adjuvant chemotherapy – trastuzumab based regimen needs to be considered for patients with Her2 positive patients.
- When AC followed by q 3weekly is being considered than the additional benefit of Paclitaxel should be questioned especially in patients with Her2 negative and ER positive patients.
- We need further data on type and benefit of chemotherapy in ER positive patients. Ongoing clinical trials such as the Tailor-x trial, prospectively evaluating Oncotype Dx test, may better predict appropriate treatment for patients with ER positive breast cancers.