Prognostic Value of Genomic Analysis After Neoadjuvant Chemotherapy for Breast Cancer

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BACKGROUND
- Neoadjuvant therapy has an important role in the treatment of locally-advanced breast cancer.
- Although a pathological complete response (pCR) following neoadjuvant therapy correlates with improved clinical outcomes, residual disease at time of surgery suggests a greater risk of recurrence and potentially implies resistance to further chemotherapy.
- The Oncotype® DX Recurrence Score® (RS) has been validated as a predictor of the likelihood of distant recurrence and likely magnitude of adjuvant chemotherapy benefit following neoadjuvant chemotherapy for hormone receptor-positive breast cancers treated with endocrine therapy.
- Use of molecular markers to optimize selection of neoadjuvant therapy is an evolving area. Data suggests that the pre-treatment RS may predict outcomes from neoadjuvant chemotherapy, including the benefit of neoadjuvant chemotherapy in the high RS group,

STUDY DESIGN AND METHODS
- Dana-Farber Cancer Institute®, DFCI) trial: 126 patients enrolled, results presented at ASCO 2010. This was a multicenter, phase II pilot study evaluating the feasibility and toxicity of post-neoadjuvant endocrine therapy in patients with residual invasive disease after neoadjuvant chemotherapy.
- Eligible patients had preoperative stage II-III invasive carcinoma, with hormone receptor positivity and HER2 negativity or low HER2 expression (HER2/NEU 0-1+). Patients were treated with endocrine therapy for 2-6 months after neoadjuvant chemotherapy. RS was determined from baseline core biopsy or surgical specimens.
- A 2008 protocol amendment allowed re-consent to inclusion of patients who were also enrolled in a pilot trial involving concurrent chemotherapy.

EXPLORATORY ANALYSES OBJECTIVES
- Comparison of the RS in Recurrence and Non-Recurrence Groups
- A total of 210 patients contributed archived FFPE tissue samples or unstained slides - 47 pre-operative biopsy core biopsies and 67 post-chemotherapy surgical samples. Of these, 34 paired pre- and post-chemotherapy samples were available. Details on the samples are described in Table 1. In general, the majority of patients were ER-positive and/or PR-positive, HER2-negative.

RESULTS
- The distribution of the RS values for patients with ER-positive tumors is similar to data from previously published series (Table 5).
- A 2005 protocol amendment allowed re-consent to inclusion of patients who were also enrolled in a pilot trial involving concurrent chemotherapy.

STUDY LIMITATIONS
- This is a relatively small, exploratory, hypothesis-generating study.
- Reasons for non-participation in this sub-analysis of the parent trial population included lack of consent from the patient or her physician to re-use tissue blocks.
- The RS sub-analysis was performed in a subset of patients who could have introduced selection bias.

SUMMARY AND CONCLUSIONS
- High RS is associated with increased risk of distant recurrence and adjuvant chemotherapy resistance. The RS may be more likely to result in pCR, this may have skewed the observed distribution of RSs.

REFERENCES

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