

## **Tissue confirmation of disease recurrence in breast cancer patients: pooled analysis of two large prospective studies.**

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**Background:** Decisions about systemic treatment of recurrent breast cancer are usually based on the estrogen (ER), progesterone (PgR), and HER2 receptor status of the primary tumor. Two recent prospective studies have investigated discordance in receptor status between the primary tumor and recurrent disease and assessed the impact of this on patient management.

**Methods:** Individual patient data from the UK BRITS and Canadian DESTINY studies were pooled. In both these studies, biopsies of recurrent lesions were prospectively obtained from consenting patients and analyzed for ER, PgR by immunohistochemistry and HER2 by immunohistochemistry and FISH. Receptor status of recurrent disease was compared to the primary tumor. Recruiting clinicians assessed whether or not receptor discordance affected subsequent systemic treatment.

**Results:** Two hundred and fifty eight patients underwent biopsy. The mean age was 60.1 years (range 27-87). Recurrent biopsy specimens were obtained from locoregional recurrence in 54% and from distant metastases in 46%. The most common sites of distant recurrence biopsy were bone (25%), liver (24%), skin (15%), bone marrow (11%), paracentesis (9%), soft tissue (6%), lung (6%) and other (4%). Discordance in ER, PgR or HER2 between the primary and recurrent disease were 13%, 28% and 5% respectively. Gain or loss of receptor expression was equally prevalent for ER and HER2, but for PgR loss of receptor was more common than gain (76% v 8%). There was no receptor discordance among triple negative primary tumors. Biopsy results altered management in 15.9% of patients (95% CI 11.7-20.9%,  $p < 0.0001$ ). The duration between primary and recurrent disease, number of prior lines of therapy and site of recurrence did not affect discordance rates.

**Conclusions:** This is the largest prospective analysis of ER, PgR and HER2 in matched primary and recurrent breast cancer and demonstrates substantial discordance in receptor status. The number needed to biopsy to alter immediate patient management was 6.3. Patients with recurrent breast cancer should have tissue confirmation of receptor status of recurrent disease.