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# Improved outcome of high-risk early HER2 positive breast cancer with high CXCL13-CXCR5 messenger RNA expression.

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## Source

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## Abstract

The CXCL13-CXCR5 is a chemokine axis that is activated in some breast cancers. A total of 321 tissue blocks from a group of patients who received adjuvant, dose-dense chemotherapy for high-risk early breast cancer were examined. Activation of this axis was found to be associated with determinants of poor prognosis but also with improved outcome in the human epidermal growth factor receptor 2 overexpressing subpopulation.

### BACKGROUND:

Chemokines are important in cell migration and are thought to play a key role in metastasis. We explored the prognostic significance of C-X-C ligand-motif (CXCL) 12, CXCL13, and receptor (CXCR) 5 on disease-free survival (DFS) and overall survival (OS) in early breast cancer.

### METHODS:

A total of 595 patients with high risk, [corrected] early breast cancer were treated in a 2-arm trial (HE10/97) with dose-dense sequential epirubicin followed by cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) with or without paclitaxel. RNA was extracted from 321 formalin-fixed paraffin-embedded primary tumor tissue samples and quantitative reverse-transcriptase polymerase chain reaction was used to assess messenger RNA (mRNA) expression of CXCL12, CXCL13, and CXCR5; estrogen receptor; progesterone receptor (PgR); microtubule-associated protein tau and human epidermal growth factor receptor 2 (HER2).

### RESULTS:

CXCL13 and CXCR5 were found to be negatively associated with estrogen receptor and microtubule-associated protein tau mRNA expression and with dense lymphocytic infiltration, and were positively associated with nuclear grade. Only CXCL13 was positively associated with HER2. Multivariate analysis revealed an association between high CXCL13 mRNA expression and improved DFS (hazard ratio [HR] 0.48 [95% CI, 0.25-0.90]; Wald, P = .023) but not OS; whereas high CXCL12 expression was significantly associated with increased OS (HR 0.53 [95% CI, 0.33-0.85]; Wald, P = .009). In the HER2 mRNA overexpressing subgroup, high CXCL13 mRNA expression was associated with improved DFS (P < .001), whereas high CXCR5 was associated with increased DFS and OS (P = .004 and P = .049, respectively).

**CONCLUSIONS:**

The CXCL13-CXCR5 axis is associated with classic determinants of poor prognosis, such as high grade, hormone receptor negativity, and axillary node involvement. Interestingly, this chemokine axis seems to be strongly associated with improved outcome in patients with HER2(+) disease.