Association of Survival With Chemoendocrine Therapy in Women With Small, Hormone Receptor–Positive, ERBB2-Positive, Node-Negative Breast Cancer

Sung Jun Ma et al

Discussion:
To our knowledge, this is the first report to suggest that there is an association between improved survival and adjuvant chemoendocrine therapy specifically for HR-positive, ERBB2-positive tumors 8
mm to 10mm compared with those smaller than 8 mm. It is evident that tumors 10 mm and smaller represent a heterogeneous group whose treatment should be tailored to improve the risk-to-benefit ratio of systemic therapy.We acknowledge the inherent challenges of diagnostic concordance in the context of millimeter-based decisions, which underscores the importance of expert pathology review.

Our study is limited by the lack of specific systemic therapy regimens. Therapy directed at ERBB2 was coded distinctly from chemotherapy during 2013 to 2015, and only 15% of such patients underwent either chemotherapy or ERBB2-directed therapy alone (data not shown). Subgroup
analysis using this cohort would be difficult because of the small sample sizes, as neither systemic therapy alone is a definitive recommendation by National Comprehensive Cancer Network in this
setting.

Postoperative readmissions and duration of postoperative inpatient admission as proxy measures for postoperative performance status were well balanced after matching. Nevertheless, while we await results of prospective trials, including the ATEMPT trial (ClinicalTrials.gov identifier,
NCT01853748), our data can help clinicians in decision-making on adjuvant systemic therapy for patients
with small HR-positive, ERBB2-positive breast cancers.

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Clinical Relevance of HER2 Overexpression/Amplification in Patients With Small Tumor Size and Node-Negative Breast Cancer

Giuseppe Curigliano et al.

Purpose
To assess the prognostic role of HER2 overexpression/amplification in patients with node-negative, pT1a-b breast cancers.

Patients and Methods
All patients with HER2-positive breast cancer were identified among a population of 2,130 patients whose diseases were staged as pT1a-b, pN0 and who underwent surgery at the European Institute of Oncology from 1999 to 2006. A matched cohort was selected by using variables of hormone receptor status, age, and year of surgery. We estimated rates of local and distant recurrence, disease-free survival (DFS), and overall survival (OS) in the two groups.

Results

We identified 150 consecutive patients with pT1a-b, pN0, HER2-positive tumors. No patient received adjuvant trastuzumab. The median follow-up was 4.6 years (range, 1.0 to 9.0 years). In the hormone receptor–positive group, 5-year DFS rates were 99% (95% CI, 96% to 100%) for HER2-negative disease and 92% (95% CI, 86% to 99%) for HER2-positive disease. In the hormone receptor–negative group, 5-year DFS rates were 92% (95% CI, 84% to 100%) for HER2-negative disease and 91% (95% CI, 84% to 99%) for HER2-positive disease. Overall, the hazard ratio (HR) associated with HER2 overexpression was 2.4 (95% CI, 0.9 to 6.5; P ? .09). After analysis was adjusted for pT1 stage, hormone receptor–positive disease with HER2-positive status was associated with a worse prognosis (HR, 5.1; 95% CI, 1.0 to 25.7). OS in HER2-positive, pT1a-b, pN0 breast cancer was similar irrespective of the hormone receptor status.

Conclusion
Patients with node-negative, HER2 positive, pT1a-b breast cancer have a low risk of recurrence at 5 years of follow-up. In patients with hormone receptor–positive disease and T1a-b, N0 tumors, HER2 overexpression was associated with a worse DFS.

A Review of the Management of T1a/bN0 HER2-Overexpressed Breast Cancer Kelly Khai Li Yap, MD, Debu Tripathy, MD

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Small node–negative breast cancers measuring less than 1 cm (pT1a/bN0) are generally associated with a favorable prognosis.

However, as many as 10% of these breast cancers exhibit human epidermal growth factor receptor 2 overexpression and/or amplification (HER2+).

Chemotherapy + trastuzumab is the accepted adjuvant therapy for early HER2+ breast cancers as it lowers the risk of recurrence and mortality, but virtually all patients enrolled in the pivotal trials for this therapy had a higher stage of disease.

Several large retrospective reviews have reported a lower overall survival among HER2+ cases in the pT1a/bN0 patient group.

The use of chemotherapy with trastuzumab has increased significantly despite the lack of direct evidence for the efficacy of trastuzumab in pT1a/ bN0 breast cancers.

This review addresses the current data regarding the prognosis of pT1a/bN0 breast cancers and outcomes of patients receiving HER2-targeted therapy.

Significant advances have occurred in the treatment of human epidermal growth factor receptor 2 (HER2)-positive breast cancer that have changed its natural history.

The addition of trastuzumab to standard therapy has dramatically improved the prognosis for patients with early stage, HER2-positive breast cancer to unprecedented survival outcomes. Yet, long-term follow-up data from adjuvant pivotal trials indicate that 15-24% of patients still develop recurrent disease. Most of the research has focused on the addition of novel anti-HER2 drugs to standard therapy, including studies evaluating the monoclonal antibody

pertuzumab; the antibody-drug conjugate trastuzumab-emtansine (T-DM1); the selective, reversible HER2/epidermal growth factor receptor kinase inhibitor lapatinib; or the irreversible pan-HER2 inhibitor neratinib.

Dual HER2 blockade has improved overall survival remarkably in metastatic breast cancer; however, in patients with early stage disease, it has led to small benefits in progression-free survival. Moreover, biologic heterogeneity within HER2-positive disease may determine response to treatment and prognosis. Different subgroups of patients with HER2-positive breast cancer may benefit from different therapeutic approaches. Thus, there is ongoing work to optimize and de-escalate treatment in patients who may do just as well with less therapy and can avoid unnecessary treatments and their related toxicities.

➤The objective of this review is to summarize the background and latest evidence on the current management of early stage, HER2-positive breast cancer and to present novel perspectives on its management.

Cancer 2018;124:4455-4466.

High Risk of Recurrence for Patients With Breast Cancer Who Have Human Epidermal Growth Factor Receptor 2–Positive, Node-Negative Tumors 1 cm or Smaller

Ana M. Gonzalez-Angulo et al.

Purpose
To evaluate the risk of recurrence in women diagnosed with T1a and T1b, node negative, human epidermal growth factor receptor 2 (HER2) –positive breast cancer.

Methods
We reviewed 965 T1a,bN0M0 breast cancers diagnosed at our institution between 1990 and 2002. Dedicated breast pathologists confirmed HER2 positivity if 3+ by immunohistochemistry or if it had a ratio of 2.0 or greater by fluorescence in situ hybridization (FISH). Patients who received adjuvant chemotherapy or trastuzumab were excluded. Kaplan-Meier product was used to calculate recurrence-free survival (RFS) and distant recurrence–free survival (DRFS). Cox propor- tional hazard models were fit to determine associations between HER2 status and survival after adjustment for patient and disease characteristics. Additionally, 350 breast cancers from two other institutions were used for validation.

Results
Ten percent of patients had HER2-positive tumors. At a median follow-up of 74 months, there were 72 recurrences. The 5-year RFS rates were 77.1% and 93.7% in patients with HER2-positive and HER2-negative tumors, respectively (P <.001). The 5-year DRFS rates were 86.4% and 97.2% in patients with HER2-positive and HER2-negative tumors, respectively (P < .001). In multivariate analysis, patients with HER2-positive tumors had higher risks of recurrence (hazard ratio [HR], 2.68; 95% CI, 1.44 to 5.0; P < .002) and distant recurrence (HR, 5.3; 95% CI, 2.23 to 12.62; P < .001) than those with HER2-negative tumors. Patients with HER2-positive tumors had 5.09 times (95% CI, 2.56 to 10.14; P < .0001) the rate of recurrences and 7.81 times (95% CI, 3.17 to 19.22; P < .0001) the rate of distant recurrences at 5 years compared with patients who had hormone receptor–positive tumors.

Conclusion
Patients with HER2-positive T1abN0M0 tumors have a significant risk of relapse and should be considered for systemic, anti-HER2, adjuvant therapy.

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