(8/9 pts, 88.9%) and pHER2− (21/45 pts, 46.7%) has been observed, while no significant difference in the rate of clinical benefit was found (p=0.24).

Conclusions: A comprehensive analysis of the patterns of expression of HER2 downstream effectors, both in pts treated with single agent H and with H-CT, is currently ongoing.

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Peritumoral lymph vascular density correlates with lymph node metastases in invasive lobular carcinoma of the breast

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Background: The most significant prognostic factor in breast cancer is the status of the axillary lymph nodes.

The presence of metastases in axillary lymph nodes may depend on the ability of the tumor to induce lymphangiogenesis. Vascular endothelial growth factor C (VEGF-C) activating vascular endothelial growth factor receptor 3 (VEGFR-3) is the major pathway for the tumor to induce lymphangiogenesis and facilitate tumor cell to disseminate into lymph vessels.

The aim of the study was to evaluate the role of lymphangiogenesis in lymphatic dissemination in invasive lobular carcinoma (ILC).

Methods: Parrafin-embedded tissue for immunohistochemical staining was obtained from 95 patients with ILC who underwent sentinel node biopsy at the Breast Surgery Unit of the Helsinki University Hospital. The tissue sections were stained with LYVE –1, VEGFR-3 and VEGF-C antibodies.

Two observers evaluated and interpreted the results of the immunohistochemical staining without knowledge of the clinical data of each patient. Estimating the percentage of tumor cells staining negative, weak positive or strong positive assessed VEGF-C staining. Tumors staining weakly positive more than 20% or strong positive more than 10% were regarded as positive.

Lymph vessel density (LVD) was assessed in three vascular hotspots by scanning the tumor at low power using a Chlakley array gratitule.

Results: The LYVE-1 positive vessels were located almost completely peritumorally. The mean LVD was 3.7 (range 0–7.3). This mean was used as a cutoff point to create two groups of low density vessel count and high density vessel count. A high LVD showed a positive correlation with the presence of lymph node metastases (P=0.01), table 1.

Table 1. Relationship between the lymph node status and tumor characteristics and VEGF-C staining and Chalkley count.

Factor	VEGFC Negative	VEGFC Positive	P	LVD low	LVD high	P
Lymph node metastasis			0.693			0.01
Negative	36 (61)	23 (39)		37 (63)	22 (37)	
Positive	17 (57)	13 (43)		9 (33)	18 (67)	
Tumor size			0.488			0.622
⩽2 cm	43 (61)	27 (39)		36 (52)	33 (48)	
>2 cm	10 (53)	9 (47)		10 (59)	7 (42)	
Grade			0.514			0.865
I	22 (56)	17 (44)		20 (54)	17 (46)	
II–III	31 (63)	18 (37)		24 (52)	22 (48)	
LVD			0.908			
low	26 (62)	16 (38)				
high	24 (63)	14 (37)				

VEGF-C staining was negative in 53 (60%) patients and positive in 36 (40%) patients.

Despite extensive testing, immunostaining by the anti-VEGFR-3 antibody resulted in unreliable staining of the vasculature and high background staining of tumoral and stromal areas.

Conclusion: There is a significant correlation between peritumoral LVD and the presence of lymph node metastases in ILC.

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Prognostic factors in breast cancer are highly influenced by the type of end-points used for relapse or survival

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Background: The reliability and clinical usefulness of prognostic factors is based on data collected in survival studies. Several definitions of end-points and competing events are used, but explicit definitions are provided in less than half of published studies.

Methods: We have studied the impact of various definitions of end-points and competing events on estimated 10-year survival in a cohort of 457 patients with primary operable breast cancer. The end-points and competing events that we used in our analyses were ipsilateral locoregional recurrent disease, contralateral breast cancer, distant metastasis, second primary malignancy, death related to breast cancer and death not related to breast cancer.

Results: The estimated survival probabilities were significantly influenced by the definition of end-points and competing events. The magnitude of this influence depended on the patient-, tumor-, and treatment characteristics of the studied population. During the median follow-up period of 10 years 30% of patients died. Thirty-six percent of all deaths were not related to breast cancer. Ten percent of deaths were observed in young patients (<50 year) as compared to 67% of deaths in the elderly (⩾70 year). The estimated 10-year relapse rate varied between 30% and 47% depending on the definition of relapse. The magnitude of the relative risk ratio between a prognostic favourable and unfavourable feature was also influenced by the definition of survival and/or relapse. The relative risk for survival depending on tumour size (⩽20 mm vs. >20 mm) was 2.57 when disease specific death was the only end-point used as endpoint, but only 1.48 when all described events were used as end-points.

Conclusions: Estimation of both survival and validity and clinical usefulness of prognostic factors depend on the definition of end-points and competing events. When prognostic factors in primary breast cancer are evaluated for survival the most appropriate definition is disease free interval with relapse defined as either locoregional recurrence or distant metastases. Non breast cancer related deaths must be censored, all other events ignored.

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Effect of HER2 and p53 expression on response to postoperative adjuvant therapy with tegafur-uracil (UFT) and tamoxifen in women with breast cancer

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Background: Meta-analysis of randomized controlled trials has shown that UFT, an oral fluoropyrimidine derivative, has a reduction in the annual odds of recurrence (RAOR) of 21% after resection in women with Stage I–IIIA breast cancer and that concomitant treatment with tamoxifen (TAM) is particularly effective (RAOR=26%). We studied the effect of HER2 and p53 expression on inhibition of recurrence by TAM monotherapy or a combination of UFT and TAM. Resected specimens obtained from patients registered in randomized controlled studies were used.

Methods: Among women registered in randomized controlled studies comparing TAM with UFT plus TAM, given as postoperative adjuvant therapy (third ACETBC trial, all women had estrogen-receptor positive tumors), those who were premenopausal and were axillary lymph node positive were studied. The expression of HER2 and p53 in tumor tissue was studied immunohistochemically with the use of anti-HER2 antibody (DAKO) and anti-p53 antibody (NOVO). Three pathologists evaluated the results in a blinded method.

Results: Tumor specimens from 192 subjects (TAM monotherapy, 97; UFT plus TAM, 95) were assessable. In the TAM monotherapy group, the rate of recurrence-free survival was significantly poorer in subjects with HER2-positive tumors than in those with HER2-negative tumors (log-rank test, p=0.0485). Similarly, the rate of recurrence-free survival was poorer in subjects with p53-positive tumors than in those with p53-negative tumors (log-rank test, p=0.014). In subjects given UFT plus TAM, there was no relation between the rate of recurrence-free survival and HER2 or p53 expression.

Conclusion: Our results suggest that the response to TAM monotherapy depends on expression of HER2 and p53, whereas that to UFT plus TAM does not depend on expression HER2 or p53.