13 samples were diagnosed with her2/neu amplification on ITC (29%). In 41 cases, both the her2/neu status of the primary tumor and on CK+ cells was available. In comparison, in 31 cases (76%) her2/neu status on the primary tumor corresponded to the her2/neu status on ITC. 7 patients (17%), however, with her2/neu overexpression or amplification on the primary tumor showed her2/neu negative ITC, whereas in 3 patients (7%) with her2/neu negative tumors we found ITC with her2/neu amplification.
Conclusion: Heterogeneity of antigen expression on the primary tumor results in a discrepancy of her2/neu status between the primary tumor and ITC in the bone marrow in a relevant subgroup of patients. Therefore, the amplification of her2/neu on persisting ITC may proof useful to stratify patients for a tailored treatment approach. New targeted agents such as her2/neu antibodies might be considered as an individualized treatment option in these patients.

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CCR7 receptor expression correlate with node involvement and survival in primary breast carcinoma

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Rationale: The role for chemokine receptors in primary breast carcinoma dissemination in regional lymph node is unclear. The expression of chemokine receptors CCR6 and CCR7 was investigated in primary breast carcinoma and tested for possible correlations with lymph node invasion and distant relapse.
Methods: CCR6, CCR7 and CCR7 ligand CCL19 expression was investigated in a prospectively collected series of 256 patients with invasive non metastatic breast cancer (NMBC) treated in the Centre Leon Berard in 1996 and 1997 (Clin Cancer Res 2004). Correlations between these markers and the characteristics of the tumors, relapse free and overall survival were analyzed in univariate and multivariate analysis. These observations were analyzed on a retrospective series of the Institute Gustave Roussy analysing the phenotype of a series of long term (>20 years) NMBC as compared to a controlled matched series.
Results: CCR7 expression was observed in 75% of tumor samples, only in non tumoral cells and mostly in fibrocytes. In univariate analysis, CCR7 expression on fibrocytes correlated to tumor size ($p = 0.001$), SBR ($p = 0.001$), node involvement ($p = 0.003$), and HER2+++ ($p = 0.01$). CCR7+ fibrocytes were also detected at the contact of tumor cells in invaded axillary lymph nodes: 16 of 32 N+ patients had detectable fibrocytes in the axillary lymp node vs 0/15 of N− patients ($p < 0.0001$). CCR7 fibrocytes were observed in the axillary lymph nodes only in patients whose primary tumors contained CCR7 fibrocytes ($p < 0.001$).
Conversely, CCR6 expression was observed in 40% of primary breast carcinoma cells. CCR6 expression on tumor cells correlated to tumor size ($p = 0.001$) and node involvement ($p = 0.02$).
CCL19 was detectable in tumor cells (57%) and in infiltrating DC (48%). CCL19 expression correlated to low SBR ($p < 0.01$), no HER2 overexpression ($p = 0.01$), and lack of ER expression ($p < 0.001$). In multivariate analysis using a logistic regression model, tumor size, CCR7 expression on fibrocytes, and CCR6 expression on tumor cells were all found to be independent predictors of nodal involvement. CCR7 expression on fibrocytes correlated to a poor relapse free (RFS) (5 year RFS: 94 vs 81%, $p = 0.01$) and overall survival (OS) (5 year OS: 97 vs 86%, $p = 0.06$) in univariate analysis, but not CCR6 expression on tumor cells.
In the IGR series, CCR7 expression also correlated to SBR grade, HER2 expression ($p < 0.01$). The proportion of long term disease free survivors was significantly higher in patients with CCR− tumors as compared to CCR7+ tumors ($p = 0.01$).
Conclusion: CCR7+ expression in primary breast carcinoma tumor is associated with a high risk of distant relapse in primary breast carcinoma.

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Prognostic effect of estrogen receptor status across age in primary breast cancer

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Background: Estrogen receptor (ER) status is the most important combined predictive and prognostic factor in breast cancer. It is well known that the chance of contracting an endocrine responsive tumor is age dependant. It is less well investigated whether the prognostic effect of ER status varies across age.
Material and methods: We used a well-established population-based registry with detailed information regarding clinical and histopathological presentation, postoperative therapy and follow-up status on Danish women with breast cancer.
Results: Overall, 26,944 patients with primary breast cancer diagnosed from 1989 to 2004 were included in the study. The chance of being ER positive increases from 51% in women < 35 yrs. to 82% in women 70–74 yrs. In a multivariate analysis ER status was found to be a significantly positive prognostic factor in women $\geqslant$ 40 yrs., but in women < 40 yrs. the survival was unaffected of ER status. The positive effect in relation to survival of being ER+ was limited to the first 5 yrs. after diagnosis, while survival after 5 yrs. was superior for women with ER− tumors. Same results were found when restricting the analysis to patients in low risk group (not receiving adjuvant therapy), n = 6,272.
Conclusion: In contrast to other studies we cannot confirm that ER+ status confer a negative impact on survival in young women. We find that the prognosis is generally worse in patients with ER− breast cancer but this applies only during the first 5 years whereafter the prognosis becomes worse in ER+ patients in the entire study group where ER status serves as a combined predictive and prognostic factor. This result stays unchanged when analyzing the untreated group separately where ER status is a prognostic factor only. This observation may be of clinical importance for future designing of adjuvant therapy beyond five years.

Oral presentations (Mon, 31 Oct, 13.45–15.45)
Large adjuvant breast cancer clinical trials relevant to clinical practice

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Doxorubicin and cyclophosphamide (AC) followed by paclitaxel (T) with or without trastuzumab (H) as adjuvant therapy for patients with HER2-positive operable breast cancer (BC): combined analysis of NSABP B-31 and NCCTG N9831

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Introduction: B-31 and N9831 are two parallel phase III randomized clinical trials evaluating the addition of H to T following AC in women with HER2+BC.
Methods: In B-31 following AC $\times$ 4, T (175 mg/m^2 q 3 w $\times$ 4) was given alone (Arm 1) or concurrently with weekly H (Arm 2). In N9831 following AC $\times$ 4, T (80mg/m^2 q w $\times$ 12) was given alone (Arm A) or concurrently with weekly H (Arm C). Both trials required normal left ventricular ejection fraction (LVEF) and negative cardiac history. All B-31 and 88% of N9831 patients (pts) had positive axillary nodes. HER2 status had to be 3+ by IHC or positive by FISH. Cardiac function was monitored by LVEF measurement at 3, 6, 9, and 18 months from randomization with strict criteria for discontinuing H due to substantial asymptomatic declines. A proposal for combined efficacy analysis (control arms 1+A vs. investigational arms 2+C) was approved in Jan. 2005.
Results: First planned interim combined data analysis in 3351 patients with follow-up showed risk reduction in disease free survival (DFS) at 3 years (yrs) of 52% (HR = 0.48, $p = 3 \times 10{-}12$) and absolute improvement in DFS of 12% at 3 yrs and 18% at 4 yrs. All subsets of pts showed strong relative benefit from addition of H. Improvement in DFS was similar across protocols. First distant recurrence was reduced by 53% with addition of H (HR = 0.47, $p = 8 \times 10{-}10$) and absolute reduction in distant recurrence was 9% at 3 yrs and 16% at 4 yrs. Distant recurrences were markedly decreased after the second year with addition of H. Relative risk reduction of death was 33% (HR = 0.67, $p = 0.015$) and absolute improvement in overall survival is 2.5% at 3 yrs and 4.8% at 4 yrs. NYHA Class III/IV CHF was 3–4% and generally responded to therapy. In the B-31 cohort 19% of pts stopped H due to symptomatic or asymptomatic cardiac dysfunction and risk of CHF correlated with post-AC LVEF and age. Review of similar data from the N9831 cohort is ongoing.
Conclusion: AC followed by TH should be considered for adjuvant therapy of women free of cardiac disease with high-risk HER2-positive BC but careful cardiac monitoring is essential when using the therapy._