performed among 69% of patients, 31% received mastectomy. Sentinel node biopsy was performed in most of cases when the axilla was clinically negative. Most of patients were post-menopausal (60%), and 99% of the tumours were hormone-responsive. The incidence of contralateral carcinoma was 1.2%, and the local recurrence rate was 5.1%.

In conclusion, ILC has a high prevalence in women in post menopause, and its biological characteristics trends to be less aggressive, although the difficulty of an early stage diagnosis exists. Conservative treatment showed to be feasible in those selected cases, and the local recurrence is not higher if compared to IDC. Sentinel node biopsy showed to be a very useful and faithful method, and should be encouraged.

297   Poster
Modified histones in breast cancer and their prognostic significance

S. El-Sheikh[1], E.A. Rakha[1], E.C. Paish[1], D.M. Heery[2], A.R. Green[1], I.O. Ellis[1]. [1]University of Nottingham, School of Molecular Medical Sciences, Nottingham, United Kingdom; [2]University of Nottingham, School of Pharmacy, Nottingham, United Kingdom

Post-translational modifications of histones are fundamental to the regulation of chromatin structure and gene activity in normal tissues. In malignant cells, aberrant acetylation and methylation of bulk histones has been reported, and similar changes have been observed at specific promoters. Alterations in histone modification have recently been shown to be predictive of clinical outcome in prostate cancer. However, the expression and prognostic significance of modified histones in breast cancer has not been previously explored. We have therefore analysed the levels of acetylated lysine 18 in histone H3 (AcH3K18) and dimethylated arginine 3 in histone H4 (diMeH4R3) by immunohistochemistry, using a large, well-characterised series of unselected breast tumours (n = 800) prepared as tissue microarrays. Immunohistochemical scoring was performed in duplicate and assessed as the percentage of positive cells. Results were correlated with clinicopathological variables and patient outcome.

Results: Absence of detection (0%) of AcH3K18 and diMeH4R3 was detected in 19.7% and 50.4% of the total cases, respectively. The detection of these histone modifications was associated with lobular and tubular carcinomas, whereas they were absent or had reduced expression (below the median) in medullary-like carcinomas. The absence of AcH3K18 and diMeH4R3 correlated with poor prognostic variables in breast cancer including; larger tumour size, higher grade, positive lymph node disease, development of recurrences and distant metastases and higher mortality rate. We also found a significant correlation of negative expression of AcH3K18 and diMeH4R3 in tumours that were negative for expression of hormone receptors, BRCA1, E-cadherin and FHIT protein, reduced luminal cytokeratins (CKs), and positive for expression of p53 and basal CKs. However, no association was found with patients' age, vascular invasion, expression of P-cadherin or members of the epidermal growth factor receptors family. Survival analyses showed that AcH3K18 and diMeH4R3 under-expression was associated with both shorter overall survival and shorter disease free interval.

Conclusion: Our results showed, for the first time that changes in specific modified histones may play an important role in breast cancer development and progression and their reduced expression is associated with poor prognosis and shorter survival.

298   Poster
Young and old age are poor prognostic factors in women with advanced breast cancer

M. De Ridder[1], G. Vlastos[2], V. Vinh-Hung[1], S. Aebi[3], G. Storme[1]. [1]AZ-VUB, Oncologisch Centrum, Jette, Belgium; [2]Hopital Universitaire, Gynecologie Oncologique, Geneve, Switzerland; [3]University Hospital, Medical Oncology, Bern, Switzerland

Background and objectives: Earlier population studies in early stage breast cancer have shown a biphasic effect of age on outcome, in which young and old age were associated with poor survival, while middle age was associated with better survival. The aim of this study was to investigate whether age has also a biphasic effect on prognosis in advanced breast cancer.

Material and Methods: Women who were diagnosed between 1988 and 1997 with histologically confirmed stage III or IV breast cancer (AJCC 3rd edition) were selected from the US Surveillance, Epidemiology, and End Results 9-registries database release 2004. Kaplan-Meier survival estimates were computed as a function of overlapping age intervals from 25 to 90 years. Odds of breast cancer death were computed relative to risk of death from other causes. Cox modeling by age-intervals were used to examine the effect of age in multivariate analyses that took into account stage, tumor location, histology, grade, hormone receptor, marrital status,

race, registry, year of diagnosis. Outcome was overall survival (OS) and breast cancer specific survival (BCSS).

Results: Out of 132,176 breast cancer in 1988–97, we identified 13,822 with advanced stage, respectively 8731 stage III and 5091 stage IV. The poorest OS (Figure 1, dashed curve) was observed in younger (<40–45 years) and in older patients (>55–60 years), the best OS in middle age patients (45–55 years). BCSS revealed a similar pattern with the best survival in middle age patients (Figure 1: plain curve). The risk of dying from breast cancer outweighed all other causes of death at all ages (odds >1 throughout the whole age range, Figure 2) and was the highest in young patients (odds 6–18 in patients <45 years, Figure 2). Multivariate analysis by OS outcome showed a hazard ratio (HR) for age adjusted by other covariates of 1.02, i.e. 2% relative increased risk of death *per each year younger than 45* (P = 0.004). By BCSS outcome, the HR was also 1.02 (P = 0.001). In patients older than 60 years, by OS outcome the HR was 1.03 (P < 0.0001), by BCSS outcome the HR was 1.01 (P = 0.0001), i.e. 1% relative increased risk *per each year older than 60*.
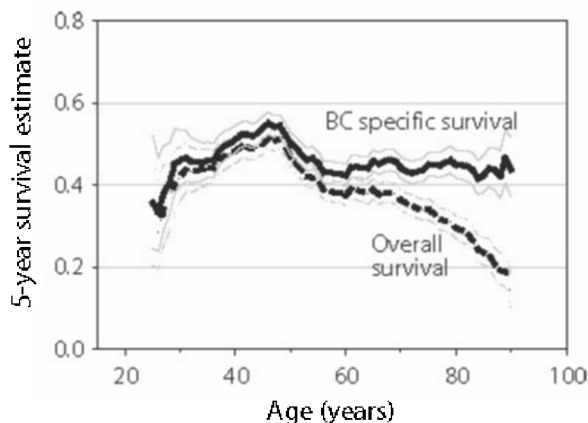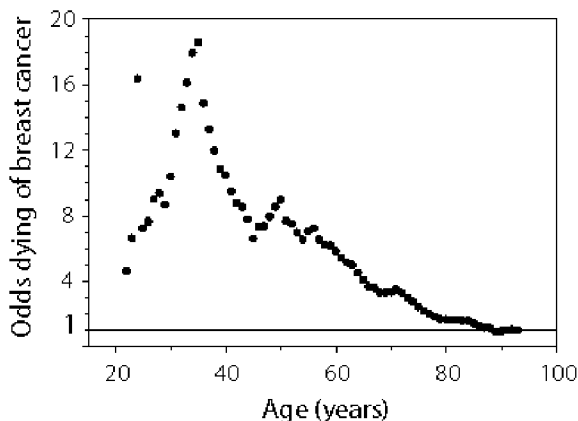

Figure 1.

Figure 2.

Conclusion: Age presents also a biphasic effect on the prognosis of patients with advanced breast cancer. Breast cancer represents a severe disease burden in young women diagnosed with advanced stage breast cancer. With older age, even though the odds decrease, the absolute risk of dying from breast cancer do not decrease and still outweighs all other causes even in 90 years old patients.