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Syndecan-1 (CD138) expression in human breast carcinoma is associated with an aggressive phenotype and appears related to a poor prognosis and low response to adjuvant chemotherapy

E. Galligioni[1], M. Barbareschi[2], D. Aldovini[2], P. Maisonneuve[3], M.G. Cangi[4], L. Pecciarini[4], O. Caffo[1], C. Arcuri[1], P. Dalla Palma[2], C. Doglioni[4]. [1]St. Chiara Hospital, Medical Oncology, Trento, Italy; [2]St. Chiara Hospital, Pathology, Trento, Italy; [3]European Institute of Oncology, Epidemiology and Biostatistic, Milano, Italy; [4]General Hospital, Pathology, Belluno, Italy

Background: Syndecan-1 is a cell-surface transmembrane heparan-sulfate proteoglycan (HSPG) which appears to play an important role in cell to cell adhesion, cell motility, invasiveness, proliferation and matrix interactions.

Material and methods: Syndecan-1 expression was investigated, by immunohistochemistry (IHC) using the B-B4 antibody, in a retrospective study on 254 consecutive infiltrating breast carcinomas (BC) (110 N0, 144 N1, 207 infiltrating ductal carcinomas, 47 special types; 46 G1, 64 G2, 133 G3, Gx 11). Among these patients, 78 were <50 years, 63 were aged 51-59 and the remaining were 60 or more years old. 80 pts were treated with adjuvant chemotherapy and 92 with hormonal therapy. Median follow-up was 86 months for disease free survival (DFS) and 95m for overall survival (OS).

Results: High Syndecan-1 immunoreactivity (>10% + cells) was seen in 42% of BC, and was associated with larger tumor size, higher grade and mitotic count, and negative ER status. High Syndecan-1 expression was related to poor DFS and OS in the whole series. Multivariate analysis in the whole series of cases unadjusted for grade showed that syndecan-1 expression was significantly and independently associated with a 1.7 fold mortality. In different age subgroups, the multivariate analysis was adjusted for grade, estrogen receptor status and lymphnodes involvement, showing that CD138 has a strong prognostic value for women aged 50-59 (p=0.0049, Risk Ratio 5.207), moderate for women <50 (p=0.1569, RR 1.850) and null for women aged 60 or more. Among patients who received adjuvant chemotherapy, a restricted model (without ER which was not significant) showed that Syndecan-1 was significantly associated with poorer OS (p=0.0345, risk ratio 2.153) along with nodal status (p=0.0569, risk ratio 6.941) and grade (p=0.0395, risk ratio 2.040).

Conclusions: Syndecan-1 is frequently overexpressed in breast carcinomas and is associated with tumor aggressiveness. It appears from our clinical data that Syndecan-1 may play an important role in human breast cancer, leading to a poor prognosis and lower response to adjuvant chemotherapy at least in some subgroups of patients.

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Risk factors for breast cancer in women residing in an urban area in the Northeast of Italy. Multivariate analysis using a logistic regression model

F. Lumachi[1], M. Ermani[2], S. Basso[1], A.A. Brandes[3], D.F. D'Amico[1], G. Favia[1]. [1]Endocrine Surgery Unit, Dept of Surg & Gastroent Sciences; [2]Section of Biostatistics, Dept of Neurosciences, University of Padua, School of Medicine, 35128 Padova, Italy; [3]Division of Medical Oncology, Azienda Ospedaliera, 35128 Padova, Italy

Introduction: Breast cancer (BC) is the most common malignancy among women in Western society, and its prevalence varies widely in different countries. Several risk factors (RF) have been reported, but none was able to give reliable epidemiological information on clinical outcome for each patient population. The aim of this study was to provide information about the relationship between BC and different RF to be considered at the time of diagnosis in women residing in the Northeast of Italy.

Patients and Methods: The study included 404 BC cases (median age 60 years, range 26-89) and 1,480 population-based age-matched controls. All patients lived in the same urban area and spontaneously underwent clinical breast examination; those with other or previous cancer were excluded. The following parameters were considered: age, family history of BC, menstrual and reproductive factors age at menarche, menstrual pattern, number of births and abortions, age at first birth) lactation, use of oral contraceptives and hormonal replacement therapy, smoking, alcohol consumption, occupational and sedentary activity, body mass index.

Results: Univariate analysis showed significant differences (p<0.01, Student's t-test and chi-squared test) between cases and controls in: (1) age at menarche (12.3±1.6 vs 12.7±1.5 years) and menopause (49.5±4.1 vs 47.3±5.3 years), (2) number of births (1.4±1.1 vs 1.8 ±1.3) and age of first birth (25.3±4.4 vs 24.4±3.6 years), (4) estrogen replacement therapy (43.9±30.3 vs 33.7±28.1 months), (5) smoking (5.94% vs 12.53%), and (6) alcohol abuse (5.69% vs 2.32%). Multivariate analysis using a logistic regression model showed that only four independent parameters correlated with BC: age at menarche (years), number of births, lactation, and estrogen replacement therapy. The Odds ratio (OR) for BC calculated from the observed vs predicted values obtained using the logistic regression function was 5.05 (95% CI 3.6-7.1), while the OR of single variables was < 3 (95% CI 1.51-4.32).

Conclusions: The results confirm that some recognized RF, such as age of menarche and the prolonged (>3 years) use of estrogen replacement therapy, are strong determinants of BC. However, in this study, many classical parameters did not result useful as RF, suggesting that to correctly select the high risk population both different primary RF and other environmental and external factors should be considered for each population.

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A comparision of young and old women with early stage breast cancer

A. Sousa[1], H. Rodrigues[2], I. Azevedo[2], H. Silva[1], C. Azevedo[2], G. Santos[1]. [1]Portuguese Institute of Oncology Porto, Department of Surgical Oncology, Porto, Portugal; [2]Portuguese Institute of Oncology, Department of Medical Oncology, Porto, Portugal

Purpose: There is controversy regarding the effect of age on breast cancer. Stages I and II breast cancer are associated with a better outcome. The aim of this study was to assess the influence of young age on outcome in women with early stage breast cancer

Methods: One hundred eight patients with breast cancer less than 2 cm submitted to surgery between March 1985 and November 1992 were divided into two age groups: a) patients with 35 years or less b) patients with more than 35 years old integrated in a breast cancer surgical protocol. The total was 108 patients being 46 young women and 62 with more than 35 years; the median age was 32 for the first group and 54 for the second. The comparability of the groups was assessed in terms of clinical factors, histological factors and treatment related factors. Outcome was evaluated for overall and disease free survival.

Results: All the 108 patients were stage I or IIa. The median follow-up was 90 months with a range of 8 to 171 months. Younger women were significantly more likely to have estrogen receptor negative tumors (37,5% versus 7,5%, p=0,003) and more nodal involvement (50% versus 27,4%, p=0,01).

95,7% of the young women had breast lumps as presentation. Patients less than 35 years were treated more often with mastectomy (65,2% versus 48,4%, p=0,08) and adjuvant chemotherapy (37% versus 11,3%, p=0,02)

For axillary node-negative women, young age was associated with a statistically significant increased recurrences (34,8% versus 11,1%, p=0,01).

There were no statistically significant differences among the two groups for overall survival; therefore there was a significant difference for disease free survival (DFS). DFS at 5 and 10 years for young women was 61% and 53% and for old women was 79% and 78% (p=0,008).

Conclusion: The present analysis demonstrates that young women with early stage breast cancer do significantly worse when compared to older women in terms of recurrences and disease free survival. Despite aggressive treatment, most commonly with mastectomy and chemotherapy, local and distant failure rates are higher in women with 35 years or less.

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Evaluation of Microtubule Associated Parameters (MTAPs) as predictive markers for Advanced Breast Cancer (ABC) patients treated with docetaxel

C. Bernard[1], A. Fellous[2], A. Di Leo[1], I. Treilleux[3], D. Gancberg[1], M.J. Piccart[1], F. Cardoso[1], M.C. Bissery[4], D. Larsimont[1], C. Dumontet[3]. [1]Inst. Jules Bordet, Brussels, Belgium; [2]Hosp. St. Louis, Paris; [3]INSERM 453, Lyon; [4]Aventis, Vitry, France

Introduction: We analyzed the possible predictive value of MTAPs regarding response to docetaxel.

Methods: A retrospective study was performed in 54 ABC women treated with docetaxel. Among the 41 eligible pts (evaluable response and available pre-treatment paraffin-embedded tumor tissue) mean age was 52 yrs (31–75), site of metastasis: visceral 76%, soft tissue 70%, bone 32%. The majority of pts received at least 1 prior line of treatment for ABC. Samples of primary and/or metastatic tumor were evaluated by immunohistochemistry for the following MTAPs: α- and β-tubulin, class II, III and IV β-tubulin isotypes, and tau protein. The clinical response was correlated with the MTAPs' status.