O-87 The role of CLEVER-1 in breast tumour metastasis

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Although the characterisation of lymphatic endothelial cells (LEC) has progressed little is known regarding the molecular events that regulate metastasis via lymphatics. We have been investigating the role of a novel lymphatic-associated adhesion molecule, CLEVER-1, in this process by assessing its expression in breast tumour specimens and by conducting in vitro experiments.

CLEVER-1 expression was examined in tonsil, lymph node (LN) and 66 breast carcinoma specimens by immunohistochemistry (paraffin-embedded sections). In vitro CLEVER-1 expression was also studied, via FACS, in HUVEC (human umbilical vein EC) and LEC (hTERT immortalised LEC) following exposure to a variety of stimuli (growth factors, cytokines and tumour conditioned media). Tumour cell and leukocyte adhesion to HUVEC and LEC were also examined.

Results show that, in tissue specimens, CLEVER-1 is present in blood and lymphatic capillaries and certain subpopulations of macrophage or dendritic cells. Although, in tumours, it is mainly expressed in blood vessels (62.1% vs 19.7% in lymph vessels) only lymphatic expression is significantly associated with LN metastasis ($p = 0.052$). Lymphovascular CLEVER-1 expression correlates with density of inflammatory infiltrate and expression in macrophage. In vitro results show that although CLEVER-1 is expressed intracellularly in both HUVEC and LEC only LEC exhibit surface expression. Interestingly, adhesion assays show that tumour cells adhere preferentially to LEC with maximal adhesion exhibited at 30–40 minutes. Such results are being further examined by using mAb blocking and siRNA knockdown along with overexpression studies to determine the role of CLEVER-1 in tumour cell adhesion and migration.

O-88 Survival of invasive breast cancer according to the Nottingham Prognostic Index in cases diagnosed in 1990 to 1999

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The Nottingham Prognostic Index (NPI) is a well established and widely used method of predicting survival of operable primary breast cancer. The index and survival figures were described in the 1982 and survival update of the original tumour set have been published with new cases added.

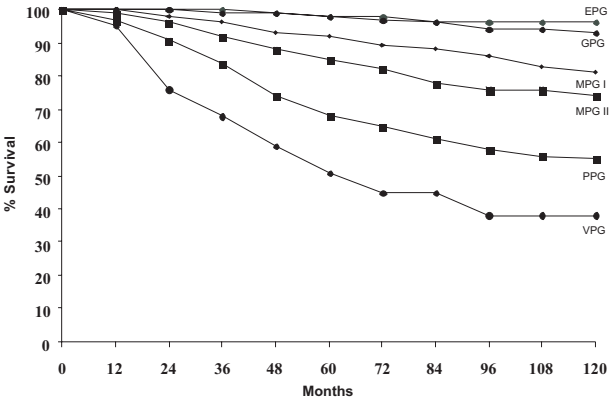
Survival in breast cancer has improved enormously and this paper presents survival figures for women diagnosed in the 1990's.

Aims: Primary: To present the survival figures for each NPI Group in women treated by up-to-date protocols. Secondary: From the observations to suggest reasons for the reported fall in mortality from breast cancer from that in the 1980's.

Methods: The NPI is compiled from grade, size and lymph node status of the primary tumour. Consecutive cases diagnosed and treated at Nottingham City Hospital in 1980–1986 ($n = 892$) and 1990–1999 ($n = 2238$) are compared. Changes in protocols towards earlier diagnosis and better case management were made in the late 1980's between the two data sets.

Results: Breast Cancer Specific Survivals are shown for each NPI group for cases diagnosed in the 1990's (Fig).

Case survival (Breast Cancer Specific) at 10 years has improved overall from 55% to 77%. Compared to cases treated in the 1980's, within all prognostic groups there are high relative and absolute risk reductions (a treatment effect). The distribution of cases to prognostic groups in the 1990's shows only a small increase from that in the early 1980's in the numbers in better groups (an early diagnosis effect).



Survival by NPI group (BCS): 1990–99.

Conclusion: Survival figures for women diagnosed in the 1990's are presented. Survival is greatly improved overall and in every prognostic group. The major part of the improvement in survival is due to improved case management with modern treatment protocols.

O-89 The effect of HER-2 overexpression on survival in early breast cancer

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Recent data suggest that there is a benefit to Her-2 testing for all patients with primary operable breast cancer as these patients may be suitable for trastuzumab therapy. Whilst there are recognized relationships between Her-2 positivity, poor prognosis and ER negativity, there is no data on the survival benefit in very early (ie Good or Excellent Prognosis) breast cancer.

Methods: Her-2 status was assessed using Herceptest and tissue microarray, in two archival consecutive datasets from the Nottingham Tenovus Primary Breast Cancer Series. The first was selected from patients (1980–1988) who received no adjuvant therapies ($n = 900$) and another from a series (1988–1995) treated with adjuvant systemic therapies ($n = 1900$).

Results: In both datasets there were no cases of HER-2 overexpression in patients in the Excellent and Good Nottingham Prognostic Index Groups. In the time period with no adjuvant therapy, the 10 year survival in the bottom three prognostic groups (ie MPG I, MPG II and PPG) was 40% vs 25% vs 14% respectively, for cases positive for HER-2 expression.

For those negative for Her-2, survival for the same period (by same prognostic groups) was 54% vs 31.6% vs 17.9%.

In those patients who received adjuvant chemotherapy, there was comparable reductions in survival even when adjusted for the influence of chemo and hormone therapy.