and C-erb-B2 (p = 0.029 and p = 0.031). In multivariate analyses axillary lenf node presence and C-erb-B2 overexpression were a strong negative prognostic factor on disease free survival and overall survival (p = 0.04, p = 0.03 for DFS and p = 0.03, p = 0.007 for OS). E-cadherin and bcl-2 failed to have an effect on disease free survival and overall survival in our study. In addition, p53 mutation positivity was observed in seven patients (9.2%), there was not any effect on prognostic parameters (p = 0.419 for DFS and p = 0.218 for OS).
**Conclusions:** The results of this study showed that E-cadherin, bcl-2, and p53 did not have any significant prognostic value for our patients. We need studies which include more patients and long follow-up periods to get a decision.

**5160** POSTER

**Long-term prognostic effects of fasting insulin in early stage breast cancer (BC) patients**

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**Background:** Hyperinsulinemia, a likely mediator of adverse prognostic effects of obesity in early BC, has been associated with increased risk of distant recurrence and/or death during the first 3−4 years after diagnosis; long-term effects are unknown.
**Materials and Methods:** An inception cohort of 512 women with T1−3, N0−1, M0 BC diagnosed at University of Toronto hospitals between 1989–1996 was followed prospectively to 2007. Tumor and treatment variables were obtained from clinical records, and women were followed for recurrence and death. Insulin was measured on fasting blood obtained postoperatively, prior to systemic therapy, using a 2-epitope immunometric chemiluminescent method (Beckman-Coulter). Distant disease-free and overall survival were analysed using Cox multivariate models adjusted for age, T stage, N stage, hormone receptors, grade, adjuvant chemotherapy and hormone therapy.
**Results:** Mean age was 50.5±9.7 years. Tumor characteristics were as follows: T1 = 287, T2 = 158, T3/TX = 59; N0 = 352, N1 = 152; ER positive = 337; PgR positive = 285; grade 1 = 73, grade 2 = 199, grade 3 = 170. Median follow-up was 11.9 years. Mean insulin level was 44.6±31.1 pmol/L. 193 (37.7%) received adjuvant chemotherapy and 197 (38.5%) received adjuvant hormone therapy. Short and long-term prognostic effects of insulin are provided in the table below. Adverse effects were present in short-term, but not long-term, analyses. Short-term effects were present in both hormone receptor positive and negative BC but were greater in hormone receptor negative BC [HR death Quartile 4 vs. Quartile 1 = 6.35, 95% CI 1.1 vs. 36.8] than in hormone receptor positive BC [HR death Quartile 4 vs. Quartile 1 = 3.03 (1.18−7.75)]. Smoothed HR curves over time show an increased risk of distant recurrence and death for the first 5 years after diagnosis, with no excess risk after 5 years.

| | Short-Term [1] (median 4.2 years) | Long-Term (median 11.8 years) | 4+ Years only |
|---|---|---|---|
| Distant recurrence HR, 95% CI Q4 vs. Q1 | 2.1, 1.2−3.6 | 1.2, 0.8−1.9 | 0.8, 0.5−1.4 |
| Death HR, 95% CI Q4 vs. Q1 | 3.3, 1.5−7.0 | 1.1, 0.7−1.7 | 0.9, 0.6−1.5 |

* Insulin Quartile 1 <27 pmol/L; Quartile 4 >51.9 pmol/L.

**Conclusions:** Adverse prognostic effects of hyperinsulinemia are seen in hormone receptor positive and negative BC in the first 4 years after diagnosis but are not present beyond 4−5 years post-diagnosis. Interventions targeting insulin should focus on the first 4−5 years post-diagnosis.

**References**

[1] Short-term effects were previously reported in Goodwin PJ et al J Clin Oncol 2002;20:42−51.

**5161** POSTER

**Clinical and pathological aspects of 90 infra-centimetric HER2+ invasive breast cancers: a 3-centres joint AERIO/REMAGUS series**

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**Background:** HER2+ and invasive infracentimetric breast carcinomas (BC) have been extensively described separately. Few fata have been published regarding the combining of both features in the same cases (InfraHER2). According to adjuvant trastuzumab (TZM) trials, InfraHER2 stand for less than 10% of HER2+ tumours. Our purpose was to describe this particular subset.
**Material and Methods:** We performed a retrospective study of patients (pts) with InfraHER2 tumours treated at 3 major French Comprehensive Cancer Centres between 2002 and 2008. Data were extracted from databases. Tumours with >80% of *in situ* component or multifocal were excluded.
**Results:** Of 90 cases listed, median age was 56 years (range 24−84). Median tumour size was 8 mm (range 2−10), 18 being ⩽5 mm (T1a). There was no significant difference in characteristics between T1a and T1b (table). Invasive ductal carcinoma (IDC) was the main histological subtype (89%). In 86 cases (96%), HER2 was overexpressed by immunohistochemistry. For equivocal cases, HER2 amplification was confirmed by FISH (range 8−20 HER2 copies). Estrogen (ER) and progesterone receptors (PgR) were expressed in respectively 44/90 cases (49%) and 22/79 cases (28%), and 19 pts (21%) had a pN+, pN0i+ or pNmi+ status. Elston-Ellis grade was III in 34% (30/89 cases) without any significant difference between T1a and T1b; 29% of tumours showed lymphovascular invasion (LVI). In one case of pN0 IDC, initial work up revealed a single bone metastatic deposit while hepatic metastases were discovered 2 years later. All patients were treated by surgery; radiotherapy, chemotherapy and TZM were delivered in 75%, 54% and 45% of pts respectively. With a 27 months median follow-up, 2 invasive recurrences have occurred. Those 2 pts had initial IDC classified as pN0, ER−, PgR− and LVI−. In one pure micropapillary case, *in situ* local recurrence occured 5 years later.
**Conclusions:** InfraHER2 tumours may present with aggressive features including node invasion, high grade or LVI, irrespective of T1a or T1b subclassification. These finding should stimulate further prospective research to assess the value of adjuvant treatment for these tumours.

| Main characteristics, N (%) | T1a (n = 18) | T1b (n = 72) | Total (n = 90) |
|---|---|---|---|
| Discovered by screening | 15 (83) | 44 (61) | 59 (66) |
| Lymphovascular invasion | 3 (17) | 23 (32) | 26 (29) |
| Elston-Ellis grade II/III | 15 (83) | 67 (93) | 82 (91) |
| Mitotic Index 2/3 | 6 (33) | 41 (57) | 47 (52) |
| ER±PgR positive | 9 (50) | 37 (51) | 46 (51) |
| pN1 (including pN0i+/mi+) | 1 (6) | 18 (25) | 19 (21) |
| Recurrence | 0 (0) | 2 (3) | 2 (2) |

**5162** POSTER

**Prognostic significance of breast cancer subtypes and nodal status**

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**Background:** To investigate the prognostic and predictive significance of subtyping breast cancer (BC) by immunohistochemistry. We analyzed and correlated breast cancer subtypes with overall survival (OS) and disease-free survival (DFS) in nodal +/− patients treated with adyuvant therapy.
**Methods:** A case series of 567 breast cancer patients treated at Granada University Clinical Hospital between 1998 and 2004 were identified retrospectively. Patients were classified by tumor characteristics as (14.5%) triple negative (estrogen receptor ER-negative, progesterone receptor PR-negative, HER2/neu HER2-negative), (8.5%) HER2 (HER2-positive, ER-negative, PR-negative), (68%) luminal A (ER-positive and/or PR-positive and not HER2-positive) and (4%) luminal B (ER-positive and/or PR-positive and HER2-positive). For mutivariante analysis, stratified cox models were built to determine de hazard ratios of breast cancer subtypes adjusting for age (median 54±11 yrs), nodal involvement (N0 62%, N1−3 24%, N > 4