as minimal response (<50% reduction in tumour volume). Changes in expression of 125 gene probes were informative in predicting for clinical response and when clustered, distinguished between responding and non-responding tumours with the exception of a single case. Whilst the ontology of the informative genes included protein metabolism (26%), transcription/translation (18%), signal transduction (14%), cell proliferation/apoptosis (14%), changes in none of the classical markers of oestrogen action and proliferation were predictive of response.

It is concluded that changes in pattern of gene expression can be detected as early as 14 days into treatment with neoadjuvant letrozole. A subset of genes allows for discrimination between tumours subsequently responding to letrozole and those that do not but these do not include classical markers.

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**Young age is not an independent prognostic factor**

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A common contention is that breast cancers in young women have worse prognoses than similar tumours in older women. In a publication (Kollias) we showed that poorer overall survival was due to the higher proportion of grade III tumours. Once standard prognostic factors had been taken into account (by use of the Nottingham prognostic Index – NPI) survival was no different from that in older women.

Survival has improved in all NPI groups in the last 15 years and the contention remains that young age is an adverse prognostic factor. A new study in tumours diagnosed 1990–99 is reported. 185 consecutive cases in women aged <40 compared with 477 cases aged 40–49 and 687 cases aged 50–59. Overall 10 year % survivals were 73, 80, 82 respectively.

Table 1. Distribution of grade and NPI at presentation (%)

| Age | Grade | | | NPI Group | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | EPG | GPG | MPGI | MPGII | PPG |
| <40 | 8 | 24 | 69 | 5 | 13 | 24 | 33 | 25 |
| 40–49 | 17 | 30 | 53 | 11 | 17 | 30 | 27 | 14 |
| 50–59 | 24 | 38 | 38 | 19 | 24 | 27 | 17 | 13 |

Table 2. Survival by NPI (10 year actuarial %)

| Group | Age | | |
|---|---|---|---|
| | <40 | 40–49 | 50–59 |
| EPG | 100 | 100 | 96 |
| GPG | 84 | 96 | 97 |
| MPGI | 78 | 78 | 84 |
| MPGII | 81 | 76 | 64 |
| PPG | 49 | 54 | 50 |

**Conclusions:**

1. Overall survival is worse in women <40.
2. Poorer overall survival is due to more grade III cases and less grade I cases in young women, placing more into the Poor Prognostic Group.
3. Survival depends on the prognostic factors of the tumour at all ages and young age is not an independent prognostic factor.
4. The difference between this report and other series may be due to the prescription of adjuvant systemic therapies: in ER positive women regardless of age at Nottingham City Hospital hormonal adjuvant therapy is the treatment of choice whereas in many centres cytotoxic therapy is used for young women.

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**Which cyclin E prevails as prognostic marker for breast cancer? Results from a retrospective study involving 635 lymph node negative breast cancer patients**

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**Purpose:** To evaluate the prognostic value of cyclin E with a quantitative method for lymph node negative (LNN) primary breast cancer patients.

**Patients and Methods:** mRNA transcripts of full length and splice variants of cyclin E1 (*CCNE1*) and cyclin E2 (*CCNE2*) were measured by real time PCR in frozen tumor samples from 635 LNN breast cancer patients who had not received neoadjuvant or adjuvant systemic therapy.

**Results:** None of the PCR assays designed for the specific splice variants of the cyclins gave additional prognosis-related information compared with the common assays able to detect all variants. In Cox multivariate analysis, corrected for the traditional prognostic factors, high levels of cyclin E were independently associated with a short distant metastasis-free survival [hazard ratio (HR) = 3.40, P < 0.001 for *CCNE1*, and HR = 1.76, *P*<0.001 for *CCNE2*, respectively]. After dichotomizing the tumors at the median level of 70% tumor cells, the multivariate analysis showed particularly strong results for *CCNE1* in the group of 433 patients with primary tumors containing 30% or more stromal components (HR = 5.12, *P*<0.001). In these tumors, the worst prognosis was found for patients with estrogen-receptor negative tumors expressing high *CCNE1* (HR = 9.89, *P*<0.001) and for patients with small (T1) tumors expressing high *CCNE1* (HR = 8.47, *P*<0.001).

**Conclusion:** Our study shows that both *CCNE1* and *CCNE2* qualify as independent prognostic markers for LNN breast cancer patients, and that especially *CCNE1* may provide additional information for specific subgroups of patients.

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**Prognosis of operable breast cancer in young patients treated in a single Institution: independent pejorative value of positive Estrogen Receptor**

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**Purpose:** According to consensus conferences for adjuvant treatments in breast cancer, young age is considered as a main criteria to justify chemotherapy. However, no multivariate prognostic analysis including clinical or biological factors has yet been published for this population.

In order to identify a good prognostic subgroup of young patients who don't require adjuvant chemotherapy, we selected in the Institut Bergonié Breast Unit database 255 patients younger than 40 whose tumors were primarily resected between 01/01/85 and 12/31/01 for a breast adenocarcinoma (group A). Characteristics of this population were compared to a group of 979 older patients (40–49) operated on at the same time (group B). A prognostic factors analysis was performed in group A.

**Results:** No significant differences were observed between the two groups for pT, rate of pN+, of ER+ and PR+. However, modified SBR grade, peritumoral emboli, mitotic count and lymphoid infiltration were significantly higher in group A. Rates of lumpectomy and adjuvant radiotherapy were similar in the two groups. Group A patients received chemotherapy more frequently (62% versus 47%) (p = 4x10–5). Considering ER+ tumors, hormonal treatment was more frequently prescribed in group B (5% vs 16% p = 2x10–4).

With a 10 year median follow-up, we confirmed a worse prognosis in younger patients: 10 years overall survival (66% vs 82% – $p = 3\times10^{-7}$), 10 years local relapse free probability (73% vs 85% – $p = 3\times10^{-4}$) and metastatic relapse free probability (60% vs 78% – $p = 2\times10^{-9}$).

Prognostic analysis of metastatic relapse in group A showed that pT2–3, pN1, peritumoral emboli, mitotic count >15 and ER+ were significantly associated with a higher metastatic relapse rate in univariate analysis. Prognostic was not significantly different between $\leqslant$ 35 and 36–39 years old patients.

Three factors remained significantly predictive of distant relapse in multivariate analysis for group A: peritumoral emboli (OR = 2.61), ER+ (OR = 2.00), and mitotic count > 15 (OR = 1.85). Ten years metastatic relapse free rate was 90%, 75%, 43% and 40% for subgroups having 0, 1, 2 and 3 of these factors; only 6% of the patients had none of these three pejorative factors.

**Conclusion:** This retrospective study confirms worse prognosis for patients younger than 40. Unlike older patients, ER positivity is associated with a worse outcome. Patients with good prognosis enough to avoid chemotherapy are uncommon before 40.