removed and this is followed by primary surgery for the breast cancer and an axillary node clearance.

**Results:** We have performed this procedure in 64 patients so far and were able to localise the SN in 61 patients (95.3%). Forty seven of the 62 patients (75.8%) had a hot node on scan and in 51 of the 61 patients (79.7%) a hot node was detected using a hand held probe. Fifty five patients had a blue node (85.9%). Twenty three patients had a positive SN. One patient who had a negative SN, had further disease in the axilla resulting in a false negative rate of 4.2%.

**Conclusion:** We conclude from our early results that the sentinel node in breast cancer can be accurately localised using a combination of methods and that it is an accurate predictor of the axillary node status. The Medical Research Council has funded a two phased, randomised trial in the UK – the ALMANAC trial – which will commence shortly.

817 PUBLICATION

## The comparative randomised study of adjuvant therapy of breast cancer patients with tamoxifen versus tamoxifen plus chemotherapy

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**Purpose:** Between 4/94 and 4/97 103 breast cancer pts, pT1c-3a, pN0-1, M0, preferably postmenopausal, were randomized after radical surgery to adjuvant tamoxifen or to tamoxifen plus CMF (C 500 mg/m$^2$, M 40 mg/m$^2$ and F 600 mg/m$^2$ days 1 and 8 q 28) for 6 cycles. The median age, tumor size, no. of involved lymphnodes (1–3), estrogen receptor status, grade and type of surgery were well balanced among the 50 tamoxifen and the 53 tamoxifen plus CMF pts.

**Results:** Toxicity either hematological and non-hematological was higher in the group with chemotherapy except weight gain (52% in both group).

| Toxicity | TAM | TAM + CMF | |
|---|---|---|---|
| Hematological | 0% | 32% | (max. leucopenia G II) |
| Non-hematological | 0% | 20% | (alopecia + cystitis + alteration of liver function) |

After median follow-up of 42 mos. 5 relapses in tamoxifen (locoregional 1, lung 1, bone 1, lung and bone 1, lung, bone and brain 1) and 7 in tamoxifen plus CMF group (locoregional 3, lung 1, bone 1, lung and bone 1, lung, bone and brain 1) were observed (p = NS). The projected 3-y DFS is 92% for tamoxifen and 88% for tamoxifen plus CMF pts. (p = NS). The 3-y OS is 88% for tamoxifen and 80% for tamoxifen plus CMF pts. (p = NS).

**Conclusions:** both regimens seems to be equale effective with higher toxicity in the group with combined hormonal and chemotherapy.

818 PUBLICATION

## The effects of adjuvant chemotherapy on alpha5-beta1 integrin expression of keratinocytes and on wound fibronectin level

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**Aim:** To evaluate the potential effects of adjuvant chemotherapy (AC) for breast cancer on wound healing at the cellular level.

**Methods:** In this prospective study, we have studied healing in an in vivo wound model. Patients with invasive, node-positive carcinoma of the breast, receiving Cyclophosphamide, Methotrexate and 5-FU were biopsied on day 8 and day 13 of the first cycle. Biopsies were snap frozen in liquid nitrogen and analysed by immunohistochemical staining. The results were compared against biopsies from age-matched healthy volunteers.

**Results:** At the time of writing, 6 patients were studied (Age range: 34–56). All wounds had healed by the end of three weeks. Wound re-epithelialisation was delayed as compared to healthy volunteers (n = 6) and the wound matrix was more friable. The alpha5-beta1 Integrin expression seemed to be unaffected in the patients receiving AC. However, the level of Fibronectin within the provisional wound matrix was found to be less than the controls.

**Conclusion:** (1) Chemotherapy does not seem to have an effect on the keratinocyte expression of alpha5-beta1 Integrin. (2) The observed decrease in the level of Fibronectin may account for the delay in wound re-epithelialisation and friability of wound matrix.

819 PUBLICATION

## Second malignancies after LH-RH analogues treatment for early breast cancer

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The appearance of new primary tumours in women operated on breast cancer and treated with adjuvant chemo and/or ormonotherapy (tamoxifen) has been described by many Authors with a 5 years incidence between 1.7 and 4.2%.

We report the experience of our Institute about 81 premenopausal women between 31 and 50 years of age with operable breast cancer treated with adjuvant Goserelin depot administered s.c. every 28 days for two years after surgery, in order to induce pharmacological castration. No patient received cytotoxic therapy before diagnosis of second primary tumour.

After a median follow-up of 60 months we observed 7 new primary tumours: 1 contralateral breast cancer, 2 chronic myeloid leukemias, 1 Hodgkin lymphoma, 1 kidney adenocarcinoma, 1 small cell lung cancer, 1 ovary cancer. All new primaries were hystologically confirmed. The second malignancies developed between 10 and 60 months after diagnosis of breast cancer. It is to be estabilished on one hand the influence of this therapy and on the other how much environmental, occupational or genetic factors could have been contributed to the development of these second tumours.

820 PUBLICATION

## Increased total dose and intensification of cyclophosphamide (C), adriamycin (A) and fluoracil (F) regimen for the treatment of breast cancer with involved nodes

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**Introduction:** The beneficial of adjuvant chemotherapy have been well established for patients (pts) with node-positive breast cancer. The intensity of the regimen is determined by the number of involved axillary lymph nodes. This study compared the combination CAF in pts with 1–3 positive nodes (pn) to sCAF in pts with 4–9 pn.

**Methods:** From December 1990 to March 1998, 79 pts with node positive breast cancer had received chemotherapy with CAF regimen. In pts with 1–3 pn the treatment consisted of C 500 mg/m$^2$, A 50 mg/m$^2$ and F 500 mg/m$^2$, every 3 weeks for 6 courses (standard CAF) and, in pts with 4–9 pn consisted of C 600 mg/m$^2$, A 60 mg/m$^2$ and F 600 mg/m$^2$ every 3 weeks for 3 courses (sCAF),

| N0 pn | Drugs (mg/m$^2$) | Dose (mg/m$^2$/wk) | Dose Intensity (mg/m$^2$) | Total dose |
|---|---|---|---|---|
| 1–3 | CAF | | | |
| | C and F | 500 | 166.6 | 3000 mg/m$^2$ |
| | A | 50 | 16.6 | 300 |
| 4–9 | sCAF | | | |
| | C and F | 600 | 200 | 3600 |
| | A | 60 | 600 | 360 |

**Results:** Median follow up was 37 months (5–81). 3 year DFS and 5 year DFS was 74% and 65% in pts with 1–3 pn and 75% and 64% in pts with 4–9 pn, respectively. A total pf 440 cycles were infused with a dose intensity >95% of 63% (CAF) and 52% (sCAF): The inceidence of WHO grade 3–4 toxicity was 6.6% with CAF and 10% with sCAF. The mayor toxicity was myelosuppresion and nausea-vomiting. Neutropenic fever was seen in 0.8% of cycles and 1 congestive heart failure was observed in sCAF group.

**Conclusion:** Total dose and dose intensity have a significant effect on DFS in the adjuvant treatment of primary breast cancer with involved nodes. SCAF is a safe regimen and may be administered over multiple cycles in ambulatory pts with excellent clinical tolerance.