

O-45. SURVIVAL AFTER DUCTAL CARCINOMA IN SITU (DCIS)

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Ductal carcinoma in situ is more frequently diagnosed due to the national screening programme. Before the onset of screening in 1988, DCIS accounted for 5% of breast cancer, but since then it has increased to 20%.

From January 1973 to December 1998, a total of 331 consecutive cases of DCIS were diagnosed, before screening 74 cases (5 per annum) and 257 (25 per annum) in the 10 years following the introduction of screening. Age range was 24–74 (median 55), 175 patients (62.8%) presented symptomatically and 120 patients were screen detected.

In 1988 a protocol was introduced for wide local excision (WLE) for tumours measuring ≤ 40 mm, with a 10 mm tumour free margin on microscopy, without radiotherapy (RT).

Dates	Protocol	n	Local Recurrence (LR)	Total deaths	Death after LR
1973–	Lumpectomy, RT	10	6	2	2
1987	Mastectomy	64	5	2	1
1988–	WLE, No RT	101	15	0	0
1998	Mastectomy	156	3	2	0

The probability of overall disease specific survival for mastectomy at 5, 10 and 20 years is 97.8%, whereas for lumpectomy or wide local excision the values are 100%, 97.5% and 86.7% respectively. Although LR occurred in only 9% of cases, 3 of the 6 deaths followed LR, emphasising the importance of local control.

O-46. STUDIES WITH IRESSA, A NOVEL EGF RECEPTOR TYROSINE KINASE INHIBITOR ON BREAST CANCER CELLS AND IN SITU CANCER “IN VIVO”

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Overexpression of EGFR and related receptors such as CerbB2 is associated with a poor prognosis in breast cancer. ZD1839 (Iressa) is an orally active, selective EGFR Tyrosine kinase inhibitor (TKI) that blocks signal transduction pathways implicated in cell growth. The effect of ZD1839 on growth of EGFR overexpression MDA-MB231 breast cancer cells “in vivo” and in situ cancer xenografts is reported.

Growth of MDA-MB231 cells allowed to form tumours over a three week period was significantly inhibited by ZD1839 by 34% and ERK MAPkinase in tumour lysates was also reduced ($p < 0.05$). A fall in Ki67 index of treated xenografts was also seen ($p < 0.01$). Epithelial proliferation in DCIS xenografts fell following 14 days of treatment from 11.7% (IQR 9.2–15.5%) to 4.6 (3.9–5.2%) ($p = 0.03$). The effect was significant at all doses from 10–200 mgs/ks body weight used. Additionally epithelial proliferation in normal breast xenografts stimulated by oestrogen

implants was inhibited from 6.2% to 1.5 ($P < 0.001$) and was associated with a fall in progesterone receptor expression from 26.8 (IQR 23.1 to 29.1) to 21.8 (IQR 18.7–23.1) $P < 0.05$ indicating inhibition of crosstalk between oestrogen receptor and EGFR pathways. This data indicates EGFR signalling is critical for the growth regulation of normal and cancer growth of the breast. Inhibition of EGFR pathways has potential for the treatment of both in situ and invasive breast cancer as well as a possible chemopreventative strategy.

O-47. LONGTERM LOCOREGIONAL CONTROL AND MORBIDITY AFTER POSTMASTECTOMY RADIOTHERAPY (PMRT)

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Significant (9–10%) survival benefits have been shown for PMRT in pre and postmenopausal women at high risk of local recurrence (LRR) in the Danish breast trials and no excess of radiation (RT) induced cardiac disease. However the Oxford overview suggests that vascular mortality largely counterbalances the survival benefit from RT.

Aim and Methods: A retrospective review from the casenotes of 188 stage 1 (24) and stage 11 (164) pre (64) and postmenopausal (124) patients who had had undergone PMRT from 1985–1989 was undertaken to assess longterm loco-regional control, survival and cardiac morbidity. Average age was 55 years (range 31–79). Primary surgery was by simple mastectomy. Axillary sampling was carried out in 147 patients, level 111 clearance in 16 and lower axillary dissection in 5.42 (22%) patients were node negative and 122 (65%) node positive. Nodal status was unknown in 21 patients. Minimum follow up was 9 years. PMRT was delivered to the chest wall (188), axilla (179) and supraclavicular fossa (185 patients). Adjuvant systemic therapy was with tamoxifen in 90 (48%), chemotherapy in 7 (4%) and oophorectomy in one patient. Overall locoregional control is summarised in the Table.

Site of relapse	% relapse at	
	5 yr	10 yr
Chest wall	15.4	20.8
Axilla	9.7	11.6
SCF	7.1	9.1

Overall 5 year and 10 year survival was 72.5% and 62.4% for premenopausal women and 63.6% and 44.7% for postmenopausal patients. For women with 1–3 N+ 5 year and 10 year survival was 67.4% and 49.1% respectively and for 4+ nodes 38.1% and 19% respectively. The proportion of cardiac deaths was as would be expected in the normal population.

Conclusions: Chest wall relapse remains the principal site of loco-regional recurrence. As in the Danish trials no excess of cardiac deaths in irradiated patients has been identified.