O-109. Therapeutic mammaplasty – approach to planning and techniques

McCulley SJ, Macmillan RD. *Nottingham City Hospital*

Therapeutic mammaplasty is the use of reduction mammaplasty techniques to treat selected breast tumours. It enables an expanded role of breast conserving surgery in cases requiring large percentage breast volume excisions, excisions in sensitive areas of the breast (central, inferior and medial) and patients with marked macromastia. Most commonly described is the use of a Wise pattern mammaplasty to remove tumours that lie within the expected mammaplasty excision. However, mammaplasty techniques can be safely adapted to treat patients with cancers in all areas of the breast. Our approach to selection and planning surgery has developed from experience with our first 50 cases. This presentation presents the technical details our approach. Techniques vary depending upon the tumour position. Breast cancers that lie within the normal excision site of a recognised mammaplasty method (scenario A) will be treated by that method without modification. Those lying beyond the expected excision sites (scenario B) require a range of techniques and modifications. Three decisions are needed for planning in scenario B; the skin incision, the nipple-aereola complex (NAC) pedicle orientation and finally the method of filling the cancer defect. The latter can be achieved by either extending the nipple pedicle or by creating a secondary pedicle within the breast dissection. Either method will move tissue that is normally excised into the cancer defect. The pedicle orientation can be from any direction.

For central tumours either a form of wedge excision or an inferior advancement pedicle is usually used to both fill the defect and recreate the nipple.

These simple principles allow a huge range of options to be employed to treat most breast tumours suitable for breast conservation. The use of therapeutic mammaplasty becomes very valuable in large percentage excisions when a poor cosmetic outcome is expected.

O-110. The growth rate of breast cancers in the observed phase according to grade

Burrell H, Blamey RW, Pinder SE. *Nottingham City Hospital*

76 breast cancers were studied. These were interval cases, which were retrospectively judged to have been false negatives at screening.

Lesions had to be measurable at both false negative and final diagnosis as a soft tissue abnormality. Cases with calcification as the main abnormality were excluded. The measurement taken was the maximum diameter on mammogram in millimetres. There was a good correlation between the size at final diagnosis and the histological size.

The overall result is given in Table 1.

Table 1

	Number	Average growth rate mm/yr
Grade 1	10	5.72
Grade 2	36	6.44
Grade 3	30	9.64

Table 2

Grade	Months
I	19.5
II	18.3
III	16.0

Taking the diameter at false negative time into account, the mean diameter doubling times were as given in Table 2.

O-111. Switching to anastrozole (ANA) vs continued Tamoxifen (TAM) treatment of early breast cancer (EBC). Updated results of the Italian Tamoxifen Anastrozole (ITA) trial

Boccardo F, Rubagotti A, Guglilmini P, Porpiglia M, Mesiti M, Rinaldini M, Paldini G, Distante V, Franchi R, Soto Para H, Buzzi F, Massidda B, Amadori D, Sismondi P, Cruciani G, Farris A and other ITA trialists. *National Cancer Research Institute & University of Genoa, Italy*

Background: Switching to ANA after 2–3 years of TAM is well tolerated and significantly improves event-free (EFS) and progression-free survival (PFS) of postmenopausal ebc (Breast Cancer Res Treat 82, 2003). Here we report on an additional analysis including 87 events and 26 deaths at a median follow-up time of 52 mos (1–80 mos).

Methods: This was an open phase III trial comparing TAM vs ANA following 2–3 years of treatment with TAM (total duration of endocrine therapy: 5 yrs) and including 448 node+ve ER+ve patients. PFS was the primary end point. EFS, OS and safety were secondary end points.

Results: The Hazard Ratios (ANA vs TAM) for EFS, PFS, local (1) PFS and distant (d)PFS are summarized in the table (Hazards of previous analysis are reported for comparison).

	Median follow-up time: 36 mos		Median follow-up time: 52 mos	
	HR (95% CIs)	$p =$	HR (95% CIs)	$p =$
EFS	0.35 (0.20–0.63)	0.0002	0.42 (0.26–0.66)	0.0001
PFS	0.35 (0.18–0.68)	0.001	0.43 (0.25–0.73)	0.001
1PFS	0.15 (0.03–0.65)	0.003	0.13 (0.03–0.59)	0.002
dPFS	0.49 (0.22–1.05)	0.06	0.57 (0.32–1.02)	0.06

17 women continued on TAM died as compared to 9 of those switched to ANA (HR: 0.52; 95% CI 0.23–1.17; $p = 0.1$). 40% and 46% of women developed at least one AE in the two groups respectively ($p = 0.2$).

Conclusions: Safety and clinical benefits of switching to ANA following 2 or 3 years of TAM are confirmed by this updated analysis.

O-112. Aromatase inhibitors (AI) versus Tamoxifen for ER-positive breast cancer – a meta-analysis

Gray R, Hills R, Shah L, Stowe R. *University of Birmingham Clinical Trials Unit*

Background: Tamoxifen treatment of ER-positive breast cancers for 5 years improves 15-year survival by almost 10 percent. AI therapy, instead of, or after the completion of standard ta-

moxifen treatment significantly improves disease-free survival. However, the improvements are small in absolute terms and the effects on breast cancer and overall mortality, and the long-term toxicity of AI treatment remain unclear. We undertook a meta-analysis of the studies of AIs to clarify the risks and benefits.

Results: AIs reduced the absolute risk of breast cancer recurrence by 2.5% (NNT 40; confidence interval 33–100; $p < 0.0001$), breast cancer death by 1.0% (NNT 110; 65–200; $p < 0.001$) and all-cause mortality by 0.7% (NNT 140; 70–700; $p < 0.05$) compared to tamoxifen. Gynaecological symptoms were fewer with AIs but osteoporosis, hypercholesterolaemia, arthralgia and diarrhoea were increased.

Interpretation: Using AIs instead of tamoxifen improves survival of post-menopausal women with ER-positive breast cancer over the first few years of treatment. However, the life years gained from AI use depend on whether the short-term benefits persist and are less for lower risk and older women. Cost/QALY appears high and switching from tamoxifen to aromatase inhibitors as first line treatment (which would cost about £70 million per year in the UK and about £1.5 billion per year worldwide) does not seem justified on current evidence. Uncertainty remains about the relative benefits and risks of aromatase inhibitors compared to tamoxifen, how the relative benefits vary over time and by background risk, whether a combination of tamoxifen and AIs is better than either treatment alone and on how long AI treatment should continue.

O-113. Aromatase inhibitors upfront: the switch of 2–5 years or extended adjuvant – how do we choose?

Cameron DA, Kerr G, Jack W, Dixon JM. *Western General Hospital, Edinburgh*

Background: The aim of the study was to identify post-menopausal patients with ER+ disease who have relapsed while taking tamoxifen in the first 2–3 years and over 5 years to identify groups of patients who should be treated either with up front AIs between 2 and 5 years, switched after 2–3 years or who should have extended adjuvant hormonal treatment.

Patients: 670 post-menopausal women with ER+ disease who were given 5 years of adjuvant tamoxifen were identified. Of these 121 have relapsed. An analysis looking for risk factors for relapse <2.5 years, 2.5–5 years and 5 years was performed.

Results: Women >70 years of age, those with ER poor tumours and those which were grade 3 or had 4 or more nodes involved were at the highest risk of relapse in the first $2\frac{1}{2}$ years. These patients should be considered for immediate treatment with AIs. From 2–5 years the rate of relapse was still high for patients with ER poor turnouts, women with grade 3 tumours and multiple node involvement. The only group who did not have a significant relapse rate in the first 5 years was patients with grade 1 cancers. Beyond 5 years, only grade and number of lymph nodes involved predicted for recurrence, such that patients with grade 2 tumours had a higher rate of recurrence than grade 1 or grade 3, and risk increased as number of involved nodes increased.

Conclusion: The study identified groups of high risk post-menopausal women with ER+ breast cancers who should be considered for immediate AIs. Thereafter analysis of relapse indicates that all other patients should be switched to an AI after 2–3 years of tamoxifen. We have also identified which women benefit from extended adjuvant therapy.

O-114. Letrozole and Anastrozole: a pre-operative study of their effects on ER positive breast cancers in postmenopausal women

Murray J, Young O, Renshaw L, White S, Prescott RJ, Krause A, Evans DB, Salem R, Cameron D, Dowsett M, Miller WR, Dixon JM. *Western General Hospital, Edinburgh*

Background: Letrozole appears to be a more potent inhibitor of oestrogen synthesis than anastrozole. Biological changes occur within 14 days of starting treatment and it is the aim of this study to investigate the changes within the first 14 days of treatment with anastrozole or letrozole.

Patients and Methods: 206 patients with 209 ER positive breast cancers (3 bilateral) were randomly allocated to receive either 2.5 mg of letrozole or 1 mg of anastrozole daily for 14 days prior to surgery. Proliferation ER, PR and Her2 were measured

Results: ER and PR: After letrozole and anastrozole treatment, there was a significant but small fall in ER (0.32, 0.20–0.44) $p < 0.0001$, and a much larger fall in PR 2.54 (2.20–2.89) $p < 0.0001$. More cases showed a reduction in PgR expression following letrozole than with anastrozole.

Proliferation: Both letrozole and anastrozole significantly reduced proliferation. Reductions in proliferation were higher in ER rich cancers, Allred 6–8 than Allred poor cancers 2–5 $p = 0.009$. There are no significant differences between the 2 drugs. Her2+ cancers had a higher initial proliferation than Her2− cancers $p < 0.003$. Both letrozole and anastrozole produced significant falls in proliferation with no quantitive differences between Her2+ and Her2− cancers. Change in PgR expression after treatment was also similar in Her2+ and Her2− groups.

Conclusion: 14 days of letrozole or anastrozole produced significant falls in proliferation and PR expression. Her2+ cancers had a higher rate of proliferation greater than Her2− cancers. Both letrozole and anastrozole produced a similar magnitude of reduction and proliferation in both Her2+ and Her2− cancers. Reduction in proliferation was greater in ER low tumours.

O-115. Is there an optimal duration of neoadjuvant letrozole therapy?

Renshaw L, Murray J, Young O, Dameron D, Miller WR, Dixon JM. *Western General Hospital, Edinburgh*

Background: Randomised studies of neoadjuvant aromatase inhibitors have treated patients for 3–4 months. The aim of this review was to assess whether tumours continue to respond to neoadjuvant letrozole for periods longer than 3–4 months.

Patients and Methods: 142 postmenopausal women with large operable or locally advanced ER rich (ER Allred score