Both procedures were performed under stereotaxis or ultrasound. Correct positioning of the wire tip or isotope was confirmed with check mammography. Analysis of results included accuracy, duration and degree of difficulty (1–10), lesion concentricity, rate of immediate re-excision and second therapeutic operation. QOL questionnaires were administered to patients following each procedure to evaluate patient perceptions.

To date 62 patients have been entered, 32 randomised to ROLL and 30 to wire-guidance. Of the 32 who had ROLL, 1 had a failed technique.

Accurate marking was 99% for ROLL and 93% for wire. Mean time for imaging was 17 minutes for ROLL and 21 minutes for the wire group. ROLL scored a median of 2 for degree of difficulty compared to 3 for wire.

Specimen x-ray analysis showed centrality of the lesion in 90% for ROLL and 83% for wire. Re-excision was higher in ROLL (13 vs 9) but the need for a second therapeutic operation was lower (23% vs 28%). Duration of operation was longer in those undergoing wire placement (37 vs 31 minutes). The median for degree of difficulty for surgery was 2 for ROLL and 4 for wire. QOL assessments showed a greater preference for ROLL over wire.

ROLL appears to be acceptable to patients quicker and easier to perform for both radiologists and surgeons compared with wire guidance. Success rates are similar.

O-7. SCINTIMAMMOGRAPHY: DOES SIZE MATTER?

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One of the major factors which determine the accuracy of breast imaging is the size of the detected lesion. This may be a particular issue in those women with dense breast in whom a small lesion may be difficult to see on mammography. The aim of this study was to review the results of Tc-99m MIBI scintimammography and x-ray mammography and compare these results with lesion size. Comparisons in accuracy were performed by comparison of area under ROC curve analysis.

Data from 273 women were reviewed were a lesion had been identified by imaging and biopsied. The mean age of the women studied was 52 with a range of 26–84 years. All patients underwent x-ray mammography, Tc-99m MIBI Scintimammography. Results of the imaging were then compared to the final histology in three size groups. Firstly in the 74 lesions of less than 2 cm the sensitivity of mammography was 51% and scintimammography 70%. In the 104 lesions sized 2–4 cm the sensitivity of mammography was 70% and scintimammography 87%. In the 52 lesions greater than 4 cm mammography found 88% of cancers and scintimammography all cancers.

Both methods have an improved sensitivity with increasing lesion size. Scintimammography was always more sensitive than mammography, however the biggest difference was in tumours of less than 2 cm when the sensitivity of scintimammography was significantly better than mammography ($p < 0.05$, Wilcoxon matched pairs). Therefore scintimammography may be of help in all women with breast cancer irrespective of tumour size but offers the biggest advantage in the smallest cancers.

O-8. UK EXPANDED ACCESS PROGRAMME (EAP): HERCEPTIN® (TRASTUZUMAB) TREATMENT FOR WOMEN WITH HER2 POSITIVE METASTATIC BREAST CANCER (MBC)

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Herceptin is a humanised monoclonal antibody against the HER2 receptor. Between 15–20% of breast cancers over-express HER2 at high levels and these patients appear to benefit most from Herceptin.

This open, non-randomised study aimed to evaluate the safety of Herceptin (H) given alone or in combination with Docetaxel (Doc.) or Paclitaxel (Pac.) in patients with HER2 positive tumours. Herceptin treatment was continued for as long as patients showed clinical benefit. Response to treatment was not formally assessed but duration of therapy was considered to be a surrogate for time to disease progression/treatment failure. All patients were ECOG PS 0-2 and could receive H as 2nd or 3rd line as single agent or 1st, 2nd or 3rd line in combination with Doc. or Pac..

From Jan to Sept 2000, 32 UK centres recruited 168 patients of whom 85 received H + Doc., 4 received H + Pac. and 79 received H alone. At end March 2001 median duration of Herceptin therapy was 5.9 months. 61 patients were still ongoing of whom 21 had received more than 9 months treatment and 7 had received more than 12 months Herceptin treatment.

Of 33 drug related SAEs reported, 8 occurred with H alone, 24 with H + Doc. and 1 with H + Pac. 4 SAEs were due to cardiac toxicity; AF on H + Doc. (2), SVT on H alone (1) and clinically significant reduced EF on H alone (1). 17 cases of myelosuppression occurred with H + Doc. One patient had a severe infusion related reaction with hypotension. In this EAP study Herceptin was generally well tolerated. Recruitment has completed and patients continue to be followed up in the study.

O-9. CORRELATION BETWEEN IMMUNOHISTOCHEMICAL AND FISH ANALYSIS FOR HER-2 IN 441 BREAST CARCINOMAS FROM MULTIPLE HOSPITALS

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The monoclonal antibody Herceptin is clinically effective in metastatic breast cancer strongly over-expressing the HER-2 oncogene. Rigorous testing procedures are required for accurate diagnosis and appropriate usage of Herceptin. Substantial controversy has surrounded the relative value of IHC and FISH for diagnosis. In particular fixation techniques and subjective scor-

ing may affect IHC, and the impact of these factors would be expected to be exacerbated in samples received from different hospitals and assessed in different laboratories. To minimize the impact of these complications in the UK, 3 sites have been identified as reference laboratories (RLs) to provide a testing service, together with training and advice. Over a period of 6 months the 3 RLs received histological sections/blocks from a total of 37 hospitals for HER-2 diagnosis in association with an "Expanded Access Programme" for Herceptin. Patients were eligible for Herceptin in the EAP if IHC2+ or 3+. A total of 468 samples were tested using the DAKO HercepTest and were categorised as negative, 2+ (equivocal) or 3+ (unequivocally positive). The overall 2+ and 3+ positivity rates were 13% (interlab range 7–19% and 24%, 23–26%), respectively. A total of 426 tumours was analysed by FISH. Only 2/270 (0.7%) of the IHC negative tumours showed gene amplification (>2-fold). Six (5.9%) of 102 IHC 3+ tumours were not amplified (>2-fold) but 5 of these had values for amplification between 1.75 and 2.0. The other had multiple copies of chromosome 17. Of the IHC 2+ tumours 48% (range 30–82%) were amplified. Thus, even in this set of tissues of various ages which had been fixed by a variety of protocols in different laboratories, the 3 RLs gave very low discordance rates between IHC and FISH in the 0 and 3+ categories. This supports the use of FISH as a secondary test in the 2+ category only.

O-10. A COST-EFFECTIVENESS ANALYSIS OF HERCEPTIN® (TRASTUZUMAB) IN COMBINATION WITH PACLITAXEL AS A FIRST LINE TREATMENT FOR HER2 POSITIVE (3+) METASTATIC BREAST CANCER (MBC) PATIENTS IN THE UK

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Herceptin has proven survival benefits in MBC patients whose tumours overexpress at a 3+ level (as determined by IHC (immunohistochemical assay). Herceptin used in combination with paclitaxel increases median survival by 39% from 18 months to 25 months[2] This is despite the poor prognosis of this sub-group: half the median survival of HER2 negative patients[1].

The objective of this analysis is to translate these clinical benefits into health economic benefits. We estimated the incremental cost per quality-adjusted life year gained (QALY) of Herceptin (in combination with paclitaxel) versus paclitaxel alone in first-line treatment of MBC patients whose tumours overexpress at a 3+ level.

The clinical trial design allowed crossover to single agent Herceptin for both treatment arms upon progression, which dilutes the estimate of the overall survival benefit. To control for this treatment switch we analysed the group of patients who did not switch treatment. For this group of patients, the addition of Herceptin to paclitaxel increased mean survival from 6.6 months (for paclitaxel alone) to 22.4 months (for the combination arm). Mean survival is therefore increased by 15.8 months, translating to 7.5 months of quality-adjusted survival. The corresponding incremental cost per life year gained is £13,400, and the incremental cost per QALY gained is £28,200.

For the 3+ HER2 positive MBC patients, Herceptin used in combination with paclitaxel has superior clinical efficacy over paclitaxel alone. The corresponding cost-effectiveness ratios are in line with other commonly used treatments recommended by the National Institute for Clinical Excellence (NICE) for use in the NHS.

References

[1] Slamon et al. 1997 Science 235: 177–182
[2] Slamon et al. 2001 NEJM 334: (11) 783–792

O-11. PHASE III TRIAL OF ANASTROZOLE (AN) vs TAMOXIFEN (TAM) IN POSTMENOPAUSAL (PM) PATIENTS (PTS) WITH HORMONE-DEPENDENT ADVANCED BREAST CANCER (ABC)

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TAM has been long been considered the gold standard therapy for hormone-sensitive breast cancer. However, since the side effects of TAM are well recognized, new drugs that lack these undesirable side effects yet conserve or improve the efficacy of TAM are needed. AN, a third-generation non-steroidal aromatase inhibitor (AI), has been shown to be a potent, selective and well tolerated agent in PM pts with ABC. In our prospective, double-blind, randomized phase III trial, we compared AN (1 mg daily) with TAM (40 mg daily) in PM pts with oestrogen receptor (ER) positive ABC. Overall response [(OR) = complete response (CR) + partial response (PR)], clinical benefit [(CB) = CR + PR + stable disease ≥ 24 weeks (SD)], median time to progression (TTP) and tolerability, the main endpoints, were evaluated after 3 months' therapy. Overall survival (OS) was assessed as the number of pts who had died within 35 months of trial initiation. A total of 238 pts were recruited and the median follow-up was 13.3 months. The efficacy results are shown in the table. The hazard ratio and confidence interval are presented for TTP and OS only. Therapy in both groups was well tolerated with a low incidence of undesirable effects.

	AN (n = 121)	TAM (n = 117)	HR, 95% CI, p values
OR [no. (%)]	41 (34)	31 (27)	p = 0 0502
CB [no. (%)]	100 (82)	65 (55)	p = 0.0287
TTP (months)	12.3	5.3	0.77, 0.56–0.91, p = 0.047
OS (%)	61	92	0.63, 0.51–0.89, p = 0.036

Our results suggest that AN is more effective than TAM in PM pts with ER positive ABC. These data are supported by the results of the North American study where 88.7% of pts overall had hormone-sensitive tumours, and TTP was significantly increase by 5.5 months (HR = 1.44, CI = 0.80–1.16, p = 0.005) in the AN arm compared with the TAM arm. Furthermore, these data are the first to demonstrate an improvement for any AI over TAM in OS.