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.