HR+EBC receiving 3 y of goserelin and (1) adjuvant ET (tamoxifen or anastrozole); or (2) adjuvant ET plus ZOL q6m. Cost-effectiveness was measured as the incremental cost per quality adjusted life year (QALY) gained. Probabilities of breast cancer recurrence were from the Austrian Breast and Colorectal Cancer Study Group Trial 12 (ABCSG-12). Other probabilities and costs specific to each country were from the published literature. Results were generated under two scenarios: (1) benefits of ZOL persist to the 7-y maximum follow-up in ABCSG-12 (trial benefit); (2) benefits persist until recurrence or death (lifetime benefit).

Results: Expected costs of 3 y of ZOL q6m (medication and administration) were €2,300 for Portugal, €2,100 for Spain, and €1,500 for Italy. Under the trial benefits scenario, these costs were partially offset by savings in treatment of breast cancer recurrence of €200 for Portugal and €900 for both Spain and Italy. ZOL was therefore projected to increase total costs by €2100 for Portugal, €1300 for Spain, and €600 for Italy. Projected QALYs gains with ZOL were 0.33 for Portugal, 0.47 for Spain and 0.46 for Italy. Cost per QALY gained was €6364 for Portugal, €2766 for Spain, and €1304 for Italy (all favorable). Assuming lifetime benefits, savings from preventing breast cancer recurrences completely offset ZOL costs for Spain and Italy, with ZOL yielding net savings of €2100 and €2900 respectively. Incremental total costs were €1400 for Portugal. Projected QALYs gains with ZOL were 0.96 for Portugal, 1.59 for Spain, and 1.57 for Italy. ZOL was therefore dominant (lower costs and more QALYs) for Spain and Italy; the cost per QALY gained for Portugal was highly favorable (€1,458).

Conclusion: Adding ZOL to ET in premenopausal women with HR+EBC is highly cost-effective (<€50,000 per QALY gained) from the healthcare system perspectives of Portugal, Spain, and Italy even under conservative assumptions regarding duration of ZOL benefits. ZOL may be cost saving in Italy and Spain if benefits persist >7 years.

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Impact of fulvestrant 500 mg/month versus fulvestrant 250 mg/month on bone turnover markers and endometrial thickness: findings from the NEWEST study

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Background: Fulvestrant (FASLODEX™) is a selective oestrogen receptor (ER) antagonist with no agonist effects used to treat postmenopausal women with advanced breast cancer at 250 mg/month (F250). Studies have suggested that increasing the dose may enhance ER blockade and improve efficacy. The NEWEST (Neoadjuvant Endocrine Therapy for Women with Estrogen-Sensitive Tumours) study compared the activity of a higher-dose fulvestrant regimen (F500, 500 mg/month plus 500 mg on Day 14 of Month 1) with F250 as neoadjuvant therapy. To collect further tolerability data for F500 vs F250, their effects on bone and endometrium were investigated.

Material and Methods: NEWEST was a Phase II, randomised, open-label, multicentre, 16-week study (9238IL/0065/NCT00093002) of F500 vs F250 in postmenopausal women with ER+, locally advanced breast cancer. Secondary objectives included comparisons of F500 vs F250 on tolerability, endometrial thickness and serum bone markers. Adverse events (AEs) were recorded throughout the study. Changes from baseline to week 16 in endometrial thickness were assessed by transvaginal ultrasound. Serum bone turnover markers (bone-specific alkaline phosphatase [ALP], C-terminal telopeptides of Type 1 collagen [CTX-1] and procollagen Type 1 N propeptide [PINP]) were measured at baseline and every four weeks until surgery (week 16).

Secondary outcome measure	n	Fulvestrant F500 (N = 107)	n	Fulvestrant F250 (N = 101)
Treatment-related SAEs, n (%)		1 (0.9)		3 (3.0)
Treatment-related AEs, n (%)		40 (37.4)		31 (30.7)
Mean change in endometrial thickness (mm), from baseline to week 16				
Patients with any baseline value	46	−1.34	44	−1.10
Patients with baseline value ⩽5 mm	37	−0.03	30	−0.18
Mean change in bone turnover markers, from baseline to week 16				
ALP (μg/L)	73	−0.36	73	−0.15
CTX-1 (ng/mL)	71	+0.02	70	+0.04
PINP (μg/L)	72	−0.35	72	+0.35

Results: In total, 211 women participated (F500 109; F250 102). Key tolerability data are shown below. Treatment-related serious AEs (SAEs) were rare; none led to withdrawal. From baseline to week 16, there were small, non-significant reductions in endometrial thickness (any baseline value) in both treatment groups. Bone turnover markers remained stable throughout the study.

Conclusions: F500 and F250 were well tolerated, with no adverse effects on endometrial thickness or bone turnover markers, indicating no ER agonist effects. The lack of impact on bone suggests a potentially good long-term tolerability profile for F500.

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First interim analysis of a randomized trial comparing capecitabine/epirubicin/cyclophosphamide (XEC) vs 5-FU/epirubicin/cyclophosphamide (FEC) as adjuvant therapy for medium- or high-risk early breast cancer (EBC)

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Background: Capecitabine is widely used as first-line therapy for metastatic breast cancer because of its high efficacy and good tolerability. Anthracyclines combined with 5-FU and cyclophosphamide are now a post-operative standard of care for medium-/high-risk EBC. We are comparing safety and efficacy of capecitabine or 5-FU combined with epirubicin and cyclophosphamide as postoperative (adjuvant) chemotherapy for EBC.

Patients and Methods: Women with node-positive or high-risk node-negative EBC are eligible for the trial. The planned sample size is 1000 patients (500 in the XEC arm, 500 in the FEC arm). The primary study objectives are to evaluate safety (NCI CTC version 3.0) and to assess 1-, 2-, and 3-year disease-free survival (DFS) rates. Overall survival is a secondary endpoint. Patients are randomised to receive either XEC (capecitabine 1000 mg/m^2 bid, d1−14 + epirubicin 75−90 mg/m^2 iv, d1 + cyclophosphamide 600 mg/m^2 iv, d1) or FEC (5-FU 500 mg/m^2 iv, d1 + epirubicin 75−90 mg/m^2 iv, d1 + cyclophosphamide 600 mg/m^2 iv, d1). In both arms, treatment is given every 3 weeks for up to 6 cycles. After completion of adjuvant chemotherapy, patients can receive radiotherapy at the investigator's discretion. Patients with hormone receptor-positive disease may receive endocrine therapy after completing adjuvant chemotherapy.

Results: By May 2009, 246 patients had been enrolled in the XEC arm and 209 in the FEC arm, all of whom are included in the intent-to-treat analysis reported here. The baseline characteristics are well balanced in the two treatment arms. After 2 years' follow-up, 1- and 2-year DFS rates are 89.24% and 61.78%, respectively, in the XEC arm, and 84.69% and 33.12%, respectively, in the FEC arm. 1-year overall survival rates are 96.03% with XEC and 93.68% with FEC. The two regimens show differing safety profiles. The incidences of all-grade adverse events with XEC and FEC, respectively, are: alopecia (6% vs 11%); hand-foot syndrome (4% vs 0%); and upper respiratory tract infection (0% vs 1%). Severe adverse events to date are neutropenia (2 cases with XEC vs 4 cases with FEC) and abnormal hepatic function (2 cases vs 0 cases, respectively). There have been no cases of severe hand-foot syndrome.

Conclusions: These interim results suggest that the risk of breast cancer recurrence can be reduced by replacing 5-FU with capecitabine in an anthracycline-based adjuvant regimen. The high activity of XEC is achieved with good tolerability.

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Pregnancy-associated breast cancer is as chemosensitive as classic breast cancer in the neoadjuvant setting

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Purpose: To determine the chemosensitivity of pregnancy-associated breast cancer (PABC) in the neoadjuvant setting.