

as Allred scores and proliferation as % Ki67 positive cells. Results are presented as means (SEM); analysis is by paired t test.

Results: ER expression fell significantly with F from a mean Allred score of 7.15 (0.25) to 4.38 (0.61), $p < 0.0001$. The fall with T from 7.21 (0.19) to 4.14 (0.98) was also significant, $p < 0.0001$. The fall in ER was significantly greater for F than T, $p = 0.02$.

PgR expression fell significantly with F from a score of 6.11 (0.47) to 4.0 (0.63), $p = 0.002$. The change with T from 6.34 (0.31) to 5.39 (0.53) was not significant, $p = 0.06$. The fall in PgR was significantly greater for F than T, $p = 0.02$.

Proliferation F reduced the mean % of Ki 67 positive cells from 14.29 (1.55) to 8.18 (1.55), $p < 0.0001$, a 48% median reduction. T reduced proliferation from 12.36 (1.71) to 4.12 (0.98), a 71% median reduction, $p < 0.0001$. Direct comparison of F and T showed no significant difference, $p = 0.06$.

HER2: 5/25 F patients were HER 2+ as were 2/29 T patients. All these 7 patients had a reduction in tumour cell proliferation.

Average pain per injection was 1.6/10. Swelling (12%), bruising (16%), and skin sensitivity (12%) were also reported at injection sites with F. Side effects with T included light headedness (10%) and hot flushes (14%). With F hot flushes (16%), loose stools (12%) and headache (28) were reported. All were grade 1 or 2. No patient contacted staff due to adverse events, before routine review.

Conclusions: In premenopausal women 750mg fulvestrant is well tolerated and significantly reduces ER and PgR expression to a greater degree than tamoxifen. Fulvestrant and tamoxifen both produce reductions in proliferation in ER+ breast cancers. Fulvestrant reduces proliferation in both HER2+ and HER2- tumors. Fulvestrant is biologically active in premenopausal women.

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Poster

Exemestane in adjuvant treatment of early breast cancer in postmenopausal women: results of a UK cost-effectiveness model

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Introduction: Standard endocrine adjuvant therapy for oestrogen positive, early breast cancer in postmenopausal women has been 5 years of tamoxifen. However, recent evidence from clinical trials shows that incorporating aromatase inhibitors into adjuvant therapy reduces recurrence rates. The Intergroup Exemestane Study (IES) has shown that switching women to exemestane, after 2 to 3 years of tamoxifen treatment, significantly improves disease free survival compared with continuing on tamoxifen. To fully evaluate the potential impact of exemestane from a policy perspective, the cost-effectiveness of switching to exemestane compared with continuing on tamoxifen has been evaluated.

Method: A decision (Markov) model was developed and adopted the UK health service perspective. The model simulates the disease progression and treatment pathway of early breast cancer over the lifetime of a female cohort. Adjuvant therapy is assumed to stop after 5 years and the model simulates the transitions among the health states: no recurrence, local recurrence, contra-lateral recurrence, distant recurrence, in remission, death from breast cancer and death from other causes. The model also includes treatment related adverse events with osteoporosis, endometrial cancer and thrombo-embolism incorporated into the model as separate health states. The main outcome measure is an incremental cost per quality-adjusted life year (QALYs) gained.

Results: Outcome analysis revealed an incremental advantage of exemestane over tamoxifen of 0.33 QALYs (13.24 v 12.91) and 0.44 (12.73 v 12.29) disease-free years. The mean total costs from the model are £7339 for exemestane and £5079 for tamoxifen treated patients. This results in an incremental cost per QALY of £6817. A probabilistic sensitivity analysis assessing the impact of variation around the key parameters was performed. This revealed that the incremental cost per QALY was less than £20,000 in 96.1% of 1000 simulations, giving confidence to our conclusion that adjuvant endocrine therapy with the switch strategy using exemestane is cost-effective.

Conclusion: Treatment with exemestane is more expensive than tamoxifen, although clinically important health gains are produced. Our model results show that switching postmenopausal women with early breast cancer to exemestane after 2 to 3 years tamoxifen is a cost-effective alternative, compared with remaining on tamoxifen for 5 years for adjuvant treatment of early breast cancer. In the future, it is anticipated that this model could be useful to policy makers in other European countries facing decisions about exemestane and other new adjuvant therapies in this area of breast cancer.

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Poster

Neoadjuvant capecitabine chemoradiation (X-RT) for patients (pts) with locally advanced breast cancer (LABC) failing anthracycline-based neoadjuvant therapy: findings from a prospective phase II trial

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Background: LABC remains a serious health problem in Brazil, it represents approximately 30% of all newly diagnosed breast cancer pts. Anthracycline-based neoadjuvant therapy is a standard treatment, but approximately 30% of pts do not respond. For these refractory pts, there is no standard approach. Retrospective data from our institution indicate that, despite receiving RT, the majority of pts still progress: only 60% became operable and the majority of pts still have gross residual disease; 4 pts have minimal residual disease (9%) and only one pathologic complete response (pCR, 4%). X is highly active and well tolerated as a single agent and extends survival, time to progression and response rates when added to docetaxel in metastatic breast cancer. Because X is a potent radiosensitizer, and it has been proven effective and well tolerated in chemoradiation for locally advanced rectal cancer, we studied the concomitant use of RT and X in pts with LABC.

Materials and Methods: Eligible pts had inoperable LABC refractory to FAC, ECOG PS 0-2 and adequate bone marrow, renal and hepatic functions. Pts received RT 50cGy/d plus X 850 mg/m² bid orally on d1-14 for 2 cycles. Pts underwent surgery, if appropriate, after completion of neoadjuvant therapy. Pts with hormone receptor-positive tumors received tamoxifen after surgery.

Results: We enrolled a total of 30 pts. Baseline characteristics were as follows: median age 47 years (range 26-70); median tumor size (after anthracyclines) 60 cm³ (range 36-357 cm³); inflammatory carcinoma (21%); hormone receptor positive tumor (ER 37.5%, PR 41%); 12 pts were HER2 2+ or 3+ (50%). Two pts were excluded from the analysis as they were protocol violators. Treatment with X-RT rendered 23 of the 28 evaluable pts (82%) operable. Four pts did not undergo surgery because of disease progression. After surgery, histology reports showed pCR in 3 pts (11%) and minimal residual disease in 4 pts (14%). A median residual tumor size of 11 cm³ (range 0-72 cm³) and a median number of positive nodes of 2 was observed. Treatment was well tolerated. The most common (all grade) adverse events were nausea/vomiting, diarrhea and mucositis. There were no grade 3/4 adverse events.

Discussion: Our data indicate that neoadjuvant X-RT is feasible, well tolerated and effective in pts with LABC refractory to FAC, rendering pts eligible for surgery. These findings suggest that a randomized study should be performed to compare RT vs. X-RT.

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Poster

Pegfilgrastim alone or with ciproflaxin significantly reduces febrile neutropenia and hospitalization vs G-CSF alone in breast cancer patients receiving neoadjuvant chemotherapy with docetaxel/doxorubicin/cyclophosphamide (TAC)

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Background and Objective: The TAC regimen (docetaxel 75 mg/m², doxorubicin 50 mg/m², cyclophosphamide 500 mg/m² on day1, q21) is frequently associated with neutropenia and neutropenia-related complications, which are the major reasons for dose delays and dose reductions. We assessed 3 consecutive patient cohorts in a prospective randomized phase 3 trial (GEPARTRIO). The objective of this analysis was to evaluate the benefits of different prophylactic growth factor regimens.

Methods: Eligible patients had T2-T4 stage primary breast cancer and were expected to receive 6-8 cycles of TAC. This analysis included data from the first 4 cycles only. Patients (n=915) were placed into 3 sequential cohorts: granulocyte colony-stimulating factor (G-CSF; filgrastim or lenograstim) on days 5-10 (n=385, 2086 cycles); pegfilgrastim 6 mg alone on day 2 (n=311, 1631 cycles); and pegfilgrastim 6 mg on day 2 plus ciproflaxin (C) (n=219, 1074 cycles). The chi-squared test was used for statistical comparisons.