O-30 Exemestane inhibits oestrogen receptor (ER) DCIS proliferation in a randomised placebo controlled trial

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Tamoxifen reduces recurrence after breast conserving surgery and radiotherapy for DCIS. No data exists on the effects of other oestrogen receptor (ER) antagonists such as Aromatase Inhibitors. Cyclooxygenase 2 (COX-2) is overexpressed in DCIS and surrounding blood vessels. Inhibition of COX-2 by Celecoxib is reported to inhibit tumour growth and angiogenesis in animal models.
We have studied the effect of Celecoxib and Exemestane, a steroidal aromatase inhibitor on epithelial proliferation, apoptosis and angiogenesis in women undergoing surgery for ER positive DCIS. Women gave written informed consent after diagnostic core biopsy and were randomised to 4 groups; Placebo, Celecoxib, Exemestane or both drugs, prior to surgery for 14 days.
Primary endpoint was fall in Ki67 between diagnostic biopsy and surgery with secondary endpoints including change in apoptosis and progesterone receptor status.
In total 90 patients were randomised, 75% were ER and Progesterone Receptor (PR) positive and 25% ER positive, PR negative. Immunohistochemistry was used to assess ER, PR, HER2, apoptosis (TUNEL) and COX-2. Initial analysis of the primary endpoint reveals Exemestane significantly reduced proliferation by 39% (HR 0.61 95% CI 0.41–0.91) compared with placebo, whereas Celecoxib did not affect proliferation. Data on apoptotic rate, PR and COX-2 expression will be presented.
Aromatase inhibition of ER positive DCIS using Exemestane appears an attractive approach to preventing DCIS recurrence after breast conserving surgery.

	n	% with >50% reduction in Ki67	%Ki67 pre-treatment	%Ki67 post-treatment
Placebo/placebo	20	20%	12.9	12.8
Placebo/celecoxib	21	24%	13.8	11.6
Exemestane/placebo	19	47%	15.5	8.1
Exemestane/celecoxib	21	43%	18.8	6.6

Exemestane $p = 0.03$; Celecoxib $p = NS$.

O-31 Anastrozole and letrozole an investigation and comparison of quality of life, tolerability and morbidity (aliquot) – results of the quality of life arm of the study

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Background: Anastrozole (A) and letrozole (L) are important non-steroidal aromatase inhibitors (AIs) which appear to be well tolerated. To date there have been no published studies using standardised measures with appropriate analyses, comparing the drugs' effects on quality of life (QoL) and how this might affect patient preferences.
Patients: 106 postmenopausal women with invasive ER +ve breast cancers were randomised to receive immediate adjuvant AI therapy after surgery with either: 12 weeks of L followed by 12 weeks of A or; 12 weeks of A followed by 12 weeks of L.
Methods: This was an open label study. QoL questionnaires the Functional Assessment of Cancer Therapy-Breast-Endocrine Symptoms (FACT-B-ES) were completed at entry, after 4 and 12 weeks of each drug. At the end of the study each patient completed a patient preference form.
Results: There was no significant difference in the overall QoL between the two drugs, and no significant change in overall FACT-ES scores or overall ES scores while patients were taking L or A. Reporting of side effects was similar for both drugs after the initial 12 weeks of treatment.
92 patients completed a drug preference questionnaire at the end of the study, 24 (26%) preferred L, 32 (35%) preferred A and 36 (39%) expressed no preference ($p = 0.296$).
12/106 (11%) patients withdrew before the end of the study for drug associated reasons, 9/102 (9%) whilst taking L and 3/95 (3%) whilst taking A.
Conclusion: Both L and A appear to be equally well tolerated and show no significant differences in overall QoL.

O-32 Predictors of early recurrence in postmenopausal women with ER+ early stage breast cancer

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Background: The use of aromatase inhibitors in the adjuvant setting reduce breast cancer recurrence compared with tamoxifen. The selection of women for aromatase inhibitor therapy remains controversial. Some patients appear particularly susceptible to early recurrence and would benefit from upfront AI therapy. Our aim was to identify this group of patients.
Methods: Data from 5 UK centres of postmenopausal women diagnosed with ER+ early stage breast cancer between 1995 and 2004, were examined. Recurrence was defined as loco-regional, contralateral or distant relapse. Univariate and multivariate surgical analysis for recurrence within 2.5 years of diagnosis was performed examining standard clinical, pathological and treatment variables. Factors that discriminated between early (<2.5 years) and later recurrence were assessed using logistic regression analysis.
Results: 4245 patients were studied. Median age at diagnosis was 62 and median follow up was 60 months. Cumulative recurrence rates at 2.5 and 5 years were 6.2% (95% CI 5.4–7.0) and 13.7% (95% CI 12.4–14.9) respectively. Increasing age tumour size, grade, nodal status, lymphovascular invasion and symptomatic presentation were independently significant predictors of early recurrence on multivariate analysis ($p < 0.01$). Increasing age (odds ratio (OR) 1.027, 95% CI 1.009–1.045, $p = 0.003$), tumour size (OR 1.57, 95% CI 1.04–2.37, $p = 0.03$) discriminated between early and later recurrence.
Conclusion: Well established prognostic variables in breast cancer were found to be strong predictors of early recurrence in this large cohort. Increasing age, large tumour size and unknown ER status discriminated between early and later recurrence and may identify a group of patients who would benefit form upfront AI therapy.