with NHR BC and evaluate overall outcome compared to younger post-menopausal pts also with NHR.

**Methods:** Retrospective study of postmenopausal pts admitted in our institution during Jan.2003–Jan.2005 with BC and NHR. Information collected from clinical records: demographic features, tumour characteristics, treatment choices, complications and results. SPSS 11.0 ® used for statistical analysis. Differences were considered statistically significant if $p < 0.05$.

**Results:** 98 pts with BC and NHR, about 15% of 647 pts admitted. 35 patients (35.7%) were ⩾65 years. Diagnosis more frequently based on symptoms for both group ages, but for pts ⩽65 yrs the percentage of asymptomatic mammography was higher ($p = 0.007$). All pts ⩽65 years had ECOG 0−1, for older pts 9.4% ECOG 2 ($p = 0.003$). More frequent comorbility in older pts ($p = 0.03$). Trend for more advanced TNM stage for older pts ($p = 0.03$). No difference between groups related to histologic type, grade or St. Gallen risk classification. Mastectomy most frequent in both groups, but conservative surgery in more younger pts. 4 pts (4.1%) not submitted to chemotherapy. In younger pts antracycline-based chemotherapy was preferred, for older pts chemotherapy not including an antracycline was more often chosen (($p < 0.0001$). Interruption of treatment more frequent after 65 yrs ($p = 0.03$). Significant toxicities did not vary between groups. After 50 months follow up 71.5% of all pts were alive, with significant difference between age groups [79.9% pts ⩽65 yrs and 45.8% ⩾65 yrs ($p = 0.04$)].

**Conclusions:** NHR BC is heterogeneous related to presentation and treatment according to age. Advanced age, worse performance status and comorbidity explain the less aggressive treatment. Advanced stage of diagnosis and less aggressive treatment relate to a higher mortality among older pts. Treatment of NHR BC in older pts is challenging, and target-therapies may have an important role.

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**Clinico-pathological features and pathological Complete Responses (pCR) to primary chemotherapy (PC)**

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**Background:** Primary chemotherapy (PC) is considered the standard of care for locally advanced or inflammatory breast cancer, but can be applied to all women who may require postoperative chemotherapy for early-stage breast cancer. Clinical and pathological responses (PR), in particular when complete, are good predictors of outcome.

**Purpose:** To correlate clinico-pathological features and pCR rates after PC, in a consecutive series of breast cancer (BC) pts.

**Patients and Methods:** Ninety four pts (median age 49 years) with stage 46 IIA (49%), 15 IIB (16%), 8 IIIA (8%), 25 IIIB (27%) BC were treated in our institution, from 2000 to 2007, with preoperative Doxorubicin 60 mg/m$^2$ and Taxol 175 mg/m$^2$ for 4 cycles, followed by 1.8 iv CMF for 4 cycles. Moreover, 11 pts with over-expressed or amplificated HER2 received concomitant trastuzumab for 8 cycles. A chi-2 test was used to evaluate the relationship between pCR rate and clinico-pathological presentation (age, menopausal status, histology, grade, ER, PgR, MIB-1, HER-2, p53).

**Results:** After PC, 45 Objective Remissions (7 CR and 38 PR) were observed (48%), while 1 pt had SD and 4 progressed. At the completion of the PC, 92 pts (98%) underwent breast conservation (64%) or mastectomy (34%); 2 pts (2%) died for causes no BC related. At definitive surgery, 16 pCR (17%) and 4 (4%) ~pCR (residual microinvasion ⩽0.1 cm) were reported, mostly in pts with rapid clinical response (after 1−2 cycles). A statistically significant correlation ($p < 0.01$) was shown between pCR+~pRC and ductal type, MIB-1 >20%, negative or low ER expression or HER2 overexpression, but not age, menopausal, stage, grading, p53 or PgR status. The pCR and ~pCR vs no pCR were significantly more frequent in ER/PR negative HER2 positive (56%) or ER/PR negative HER2 negative (33%) or ER/PR positive HER2 positive (35%) subsets, rather than in ER/PR positive HER2 negative (8%) pts. The 36 months DFS and OS are 94% and 84% respectively, with all pCR pts alive and relapse free and only 1 ~pCR pt relapsed and died.

**Conclusions:** In our study, as in the literature, pts with ductal histology and low or absent ER and/or positive HER-2 expression, appear to benefit more from PC. For pts with lobular histology and positive ER and negative HER2 expression, alternative strategies, such as a neoadjuvant hormone-therapy, should be considered.

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**Anastrozole shows greater carryover effects compared with tamoxifen and resolution of fracture risk post-treatment – data from ATAC at 100 months' median follow-up**

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**Background:** ATAC showed that anastrozole (A) is significantly more effective than tamoxifen (T) in preventing recurrences and is better tolerated but associated with a higher risk of fractures on treatment. Little data exist on whether effects persist after aromatase inhibitor (AI) treatment is completed. Data from ATAC at 100 months' median follow-up are presented.

**Material and Methods:** The primary endpoint, disease-free survival (DFS), and secondary endpoints, time to recurrence (TTR), incidence of new contralateral breast cancer (CLBC), time to distant recurrence (TTDR), overall survival (OS) and death after recurrence, were assessed in the total (ITT) and hormone receptor-positive (HR+ve) populations (84% of ITT). After treatment completion, fractures and serious adverse events (SAEs) continued to be collected in a double-blinded fashion.

**Results:** Significant improvements were seen for A over T for DFS, TTR, TTDR and CLBC. In the HR+ve group: DFS (HR 0.85; 95% CI 0.76, 0.94; $p = 0.003$), TTR (HR 0.76; 95% CI 0.67, 0.87; $p = 0.0001$) TTDR (HR 0.84; 95% CI 0.72, 0.97; $p = 0.022$), and CLBC (HR 0.6; 95% CI 0.42, 0.85; $p = 0.004$). Absolute benefit of A over T continued to increase over time (TTR 2.8% at 5 yrs; 4.8% at 9 yrs) and recurrence rates remained significantly lower on anastrozole compared with tamoxifen after treatment completion (HR 0.75; 95% CI 0.61, 0.94; $p = 0.01$). Deaths following recurrence were non-significantly fewer with A than T (245 vs 269) but there was no difference in OS (472 vs 477; HR 0.97; 95% CI 0.86, 1.11; $p = 0.7$). After treatment completion, fracture rates fell for the A-treated patients and post-treatment rates were similar in both groups (annual fracture rate A 146 [1.56%] vs T 143 [1.51%]). Treatment-related SAEs were lower on A during treatment and similar between A and T after treatment completion.

**Conclusions:** Analysis of ATAC at 100 months is the longest median follow-up for initial AI 5 years' treatment to date. The data shows that following completion of treatment, the efficacy benefit of A over T continues and there is statistically significant evidence of a greater carryover effect for A compared with T. These data represent the first demonstration of a carryover effect for an AI. Fracture rates for A and T are similar after cessation of therapy. No statistically significant difference in OS is observed in this study, in which there are competing causes of mortality.

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**Comparison of the cost-effectiveness of upfront letrozole or anastrozole versus tamoxifen for early breast cancer in hormone receptor positive (HR+) postmenopausal women – the Cypriot perspective**

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**Background:** The BIG 1-98 and ATAC randomized controlled trials demonstrated that, in postmenopausal women with hormone receptor positive (HR+) early breast cancer, initial adjuvant therapy for 5 years with the aromatase inhibitors (AIs) letrozole (LET) or anastrozole (ANA) is superior to tamoxifen (TAM). Previous economic analyses modelled constant hazard rates for recurrent events, which did not reflect the observed variation over the five year treatment period. This study reflects the observed time dependency in hazard rates by recurrence type to evaluate the incremental cost per quality-adjusted life year (QALY) gained with five years of initial adjuvant therapy with LET or ANA versus TAM in postmenopausal women with HR+ early stage breast cancer, from a Cypriot perspective.

**Methods:** The analysis used the same Markov model structure used in the independent assessment conducted for the National Institute for Clinical Excellence (NICE) in the. A pooled set of variable annual hazard rates for TAM were estimated, to which were applied variable annual hazard ratios for time to recurrence for the 5 year treatment period estimated from the BIG 1-98 and ATAC trials for LET and ANA, respectively. Probabilities of breast cancer event type (contralateral; locoregional; soft tissue, bone, and visceral metastases) and Adverse Events (endometrial cancer, hip fractures, stroke, thromboembolic events, and vaginal bleeding) were based on published results of the BIG 1-98 and ATAC trials and population-based studies as appropriate. Treatment costs for AEs, and health-state utilities (QALY weights) were obtained from primary studies. Resource use for treating recurrent breast cancer was informed by a survey of clinicians,

to which Cypriot unit costs were applied. Costs and QALYs were estimated over the remaining lifetime of a cohort of HR+ women aged 60 yrs, discounted at 3.5% annually.

**Results:** LET and ANA are predicted to increase QALYs by 0.32 and 0.23 per patient compared to TAM, respectively. Lifetime costs increase by CYP 651 and CYP 841, respectively. The mean incremental cost per QALY (ICQ) gained of LET vs TAM is CYP 2,067 (95% CI LET dominates – CYP 6,382), and of ANA vs TAM is CYP 3,633 (95% CI CYP 803–9,340). This suggests (based on the difference in mean values) LET is more cost-effective than ANA, providing a 40% reduction in the cost-effectiveness ratio. The probabilistic sensitivity analysis shows that LET and ANA have around a 100% probability of being cost-effective at a QALY value of CYP 20,000.

**Conclusion:** Compared to TAM, adjuvant treatment of postmenopausal HR+ women with LET or ANA for 5 years is a cost-effective use of Cypriot health care resources. Comparing mean values LET is more cost-effective than ANA, although the confidence intervals overlap.

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**Patient's Anastrozole Compliance to Therapy Programme (PACT) influence of the addition of a standardized information and reminder service on compliance in comparison to standard clinical care alone in women with early breast cancer**

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**Introduction:** An important requirement for the effectiveness of any therapeutic intervention is optimal compliance. The level of compliance to oral pharmacological therapies in chronic diseases vary, but are predominantly low. In the adjuvant treatment of hormone responsive breast cancer, existing data document that 23% and 50% of patients were non-compliant after the first and fourth year of tamoxifen (TAM) therapy. To date, no data on compliance to aromatase inhibitors (AI) outside of randomized clinical trials (RCTs) has been reported.

**Design:** PACT program has a two arm, randomized, parallel group design with a primary duration of 12 months and observation extended to 60 months. From July 2006 to September 2008, we intend to enrol 4.674 postmenopausal, receptor positive breast cancer patients assigned to adjuvant AI therapy in accordance with standard local practice and independent of participation in the program. After written informed consent, patients will be randomized to a standardized information and reminder service or to routine clinical care alone. Compliance will be evaluated by self report using standardized, detailed questionnaires at baseline and after each year of treatment. In addition, we will collect the prescription data for each patient from hospital records and physician recall. Finally, we will assess quality of life and patient's satisfaction using standardized questionnaires. Secondary endpoints include persistence on therapy, reasons for non-compliance, influence of baseline characteristics on compliance as well as the influence of compliance on clinical outcome parameters.

**Future perspectives:** An important goal of any therapeutic intervention is to achieve comparable efficacy in routine clinical practice to that demonstrated in RCTs. The aim of the PACT program is to evaluate whether a simple intervention such as a standardized information and reminder service can lead to a significant increase in compliance in women with primary breast cancer. If successful, such simple measures could greatly improve the efficacy of adjuvant endocrine treatment and would thus have significant impact on individual patient outcomes as well as the health care system.

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**Results of the German IPEP study evaluating the tolerability, efficacy, and acceptance of fulvestrant (Faslodex®) under routine clinical conditions in advanced breast cancer**

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**Background:** Fulvestrant is used in the treatment of postmenopausal women with estrogen receptor-positive, locally advanced or metastatic breast cancer. The questions of the study are whether Fulvestrant is safe, effective and tolerable.

**Material and Methods:** 848 patients were enrolled in this Fulvestrant In Practice Evaluation Programme (IPEP). Under clinical routine conditions in the participating centers regarding selection of subjects, diagnostic procedures or therapeutic decisions, all relevant data was documented over 9 months of fulvestrant therapy in postmenopausal women with advanced ER+ breast cancer who had relapsed during or after adjuvant anti-estrogen treatment, or with disease progression under palliative anti-estrogen therapy.

**Results:** Data of 597 (70 %) of patients was evaluable according to protocol. Median age was 64 years, 52% of patients had a co-morbidity, 78% one or more prior palliative therapies. *Safety*: 15.6% had one or more adverse events, mainly hot flushes, gastrointestinal, or musculo-sceletal symptoms, 27 patients had a serious adverse event, 20 died during observation. *Efficacy*: after 3 months only 11.5% of patients had progressed; 6% had a complete remission, 16.5% partial remission, 58% stable disease as locally assessed by the investigators. After 9 months, 15% of evaluable patients had progressed, 13% were in complete remission, 28% in partial remission und 42% had stable disease, 2% are not available. *Tolerability*: Tolerability was judged as being good to very good by the majority of both investigators and patients with stable tolerability parameters reported at 3, 6 and 9 months (Patients "very good": 43.5%, "good": 48%. Specialists "very good": 48%, "good": 46%).

**Conclusions:** Overall, fulvestrant showed very good efficacy with a reported clinical benefit rate of 83% after 9 months, safety and tolerability in this observational study in a patient collective with advanced breast cancer.

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**Local recurrences are not increased in patients who undergo breast conservation after neoadjuvant chemotherapy**

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One of the benefits of neoadjuvant chemotherapy is its ability to convert patients ineligible for breast conservative treatment (BCT) to be candidates for this treatment. Although it has not been shown to increase survival, questions have been raised regarding the effectiveness of BCT in terms of local recurrences. The objective of this study is to determine rates of mastectomy conversion to BCT and to evaluate the local recurrences in this group of patients.

Between 1995 and 2005, 214 patients with breast cancer were treated with neoadjuvant chemotherapy at our institution. Median age was 57.2 years old (range, 25 to 94 years old). Clinical stage at diagnosis was I in 2.9%, II in 53.2%, and III in 43.9%. After completion of chemotherapy a multidisciplinary team evaluated the cases eligible for BCT. All patients treated with BCT had negative margins and received radiation therapy as part of the conservative treatment.

Sixty patients (29.3%) candidates for mastectomy received BCT after neoadjuvant chemotherapy. At a median follow up of 50 months (range, 16 to 144 months), 19 patients developed local recurrences, 5 (8.3%) were ipsilateral breast recurrences in the BCT group. Twenty patients (9.8%) developed distant metastasis, 3 (5%) of these in the BCT group. There were 2 patients who developed a metastasis after a local recurrence. Both patients have had a modified radical mastectomy. None of the patients who developed ipsilateral local recurrences had a pathologic complete response after surgery. Variables as tumor size, or vascular invasion were not associated with ipsilateral breast recurrences. Five-year actuarial ipsilateral local recurrences-free survival rate was 92%.

The results of this study not only confirm the advantage of neoadjuvant chemotherapy in allowing BCT in patients who otherwise would require a mastectomy, but also have showed that rates of local recurrences-free survival compare favourably to those for patients with adjuvant chemotherapy. BCT is a safe and feasible treatment in patients with neoadjuvant chemotherapy.