**237** Invited

**Individualised systemic treatment**

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Prognosis of locally advanced breast cancer (LABC) has been substantially improved since the introduction of neoadjuvant chemotherapy (NAC) in the late 70s. With anthracycline based NAC, 10-year survival rates of pts with LABC rose to 23–50%, with a pathologic complete remission (pCR) being an excellent predictor of long-term survival. During the last few years progress was made through the incorporation of new drugs and manipulation of dose-size and dose-density of cytotoxic agents. NSABP B27 and Aberdeen trial showed that the addition of taxanes to anthracyclines can further improve pCR rates and maybe even survival in LABC, with benefits mostly confined to pts responding to anthracyclines; dose-dense, biweekly as well as weekly applications of paclitaxel resulted in higher pCR rates in AGO and MDACC trial; higher cumulative dose of both anthracycline and taxane resulted in higher pCR in a large GEPARDUO trial. These developments already help clinicians to individualize and improve treatment strategies. There is evidence coming from LET 024 trial and some smaller studies, that in HR+ disease response rates can be increased by substituting tamoxifen with a new generation of AIs; however, pCR rates remain low and use of neoadjuvant HT is still limited to unfit, older patients. There are limited observations on different efficacy of AIs and tamoxifen in HER2+ disease and on predictive value of Ki67 changes for response to AIs, which still need to be tested in a prospective manner. Not surprisingly, the addition of trastuzumab to NAC in HER2+ disease resulted in encouraging pCR rates ranging from 18–41% in phase II trials, with an astonishing doubling of pCR rates to 65%, achieved with trasuzumab and anthracycline-taxane combination, in prematurely stopped phase III trial. Further progress can be achieved by the introduction of additional new targeted drugs and by the incorporation of individualized treatment strategies based on molecular markers of response. Evidence exists that women with ER-negative, grade 3, highly proliferative tumors derive larger benefits from NAC; and there are some retrospective observations that some molecular markers such as HER2, topo II and p53 may predict for sensitivity to antracyclines and taxanes, the hypotheses being currently tested in prospective manner in the TOP and EORTC p53 trials. Based on gene expression profiling breast cancer may be subclassified into luminal, basal, and HER2 subtypes, with distinct differences in prognosis and response to therapy; by IHC determination of three markers ER, PR and HER2, it is already possible to distinguish breast cancer subclasses that respond differently to systemic therapy. Studies showing that gene expression profiling may be useful to predict response to neoadjuvant therapy are of great importance; but there is still a long way to go before we will be able to use individualized therapy in each particular patient.

**238** Proffered Paper Oral

**Primary endocrine therapy vs chemotherapy in postmenopausal ER-positive breast cancer patients**

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**Background:** before this trial there were few direct comparisons of primary (neoadjuvant) endocrine therapy with primary chemotherapy in breast cancer patients. However, there are suggestions that the activity of preoperative chemotherapy may be reduced in postmenopausal (PM) patients with ER and/or PgR positive tumors, as least with respect to doxorubicin or taxanes-containing regimens.

**Patients and Methods:** 239 PM women with ER+ and/or PgR+ breast cancer (BC) T2N1–2, T3N0–1, T4N0M0 (excluding inflammatory cases) were randomly assigned primary treatment with either endocrine therapy with aromatase inhibitors, n = 121 pts (once daily anastrozole 1 mg, n = 61; or exemestane 25 mg, n = 60) 3 month, or chemotherapy (doxorubicine 60 mg/m$^2$ + paditaxel 200 mg/m$^2$) every 3 weeks, 4 cycles, n = 118 pts.

The primary endpoint was to compare overall objective response (OR) determined by clinical (palpation), mammography and ultrasound. Secondary endpoint was the number of pts who qualified for breast-conserving surgery (BCS) + radiotherapy (50 Gy for 25 fractions).

**Results:** Clinical OR was statistically similar in the endocrine and chemotherapy groups (Gr) [62.2% vs 63.5%, p > 0.5]. Median time to clinical response was 57 days in the endocrine Gr and 51 days in the chemotherapy Gr (p > 0.05). A pathological CR was shown in 3.2% pts endocrine Gr and 5.9% pts of chemotherapy Gr (p > 0.05). Progression were observed in 9.0% pts of endocrine Gr and 8.5% pts of chemotherapy Gr (p > 0.5). In chemotherapy arm the most frequent grade III/IV toxicity was alopecia (79%), neutropenia (33%), neuropathy CTC 2 (30%). Endocrine treatment was well tolerated. No death occurred during the preoperative treatment.

**Conclusion:** This trial have shown that preoperative endocrine therapy with aromatase inhibitors (anastrozole or exemestane) offers the same rate of overall OR and BCS as does chemotherapy (doxorubicine + paclitaxel) in PM with ER+ tumors. The frequency of adverse events were higher in chemotherapy group. Hormonal treatment was well tolerated.

## Thursday, 23 March 2006 14:15–16:00

**SCIENTIFIC SESSION**

# Hormonal replacement therapy and alternatives

**239** Invited

**New perception of benefits and risk of HRT**

Abstract not received.

**240** Invited

**Overview of trials done in breast cancer – what have we learned?**

H. Olsson. *Lund University Hospital, Department of oncology, Lund, Sweden*

A subset of healthy women and breast cancer patients have a need for hormone replacement therapy. Observational studies (case-control and cohort studies) as well as data from a randomized trial consistently have found an increased risk for breast cancer after combined HRT use. The overall cancer incidence in HRT users are not increased. For estrogen or tibolone only use results suggest a low or nonexisting risk for breast cancer. Data on tibolone is limited and there is a need for more data provided by the ongoing randomised trials. Results are inconsistent to whether prognosis of breast cancer is affected by previous HRT therapy. The only modifying risk factor seems to be body weight.

While observational studies suggested that HRT could be given with low risk to breast cancer patients data from the randomised HABITS trial clearly showed an adverse effect from combined HRT use on breast cancer recurrence and risk for new contralateral breast tumours. The predominant type of HRT used was continuous combined, while data on sequential combined HRT, used in the Stockholm trial, did not show an adverse effect in breast cancer patients. It is therefore unclear if sequentially given combined HRT is a safe alternative for breast cancer patients. A trial addressing this hypothesis will probably be difficult to launch in the future. Whether it is safe to give tibolone to breast cancer patients awaits the results of an on going trial (Liberate trial). The safety committee has, so far, not found reasons for stopping the trial and the first official results will be available in 2007. Research data on the safety of low dose IUDs or progestin spaced every 3 month and oral estrogens are urgently needed as well as more data on the use of natural progesterone. It is possible that surrogate measures of breast cancer risk such as breast tenderness, breast density or breast tissue proliferation could guide the use of HRT in the invididual woman. Ultimately blood tests (gene or protein based) will be developed to guide therapy options.

Menopausal health will continue to be an important issue for women decades onwards and the medical research community has an obligation to provide hormone therapy as safe as possible.

While there is no reason for advocating HRT use for nonsymptomatic women it is unclear if there is real good non hormonal alternatives for women with severe menopausal symptoms.

**241** Invited

**Alternatives to hormonal replacement therapy (HRT): what are the evidence-based alternatives?**

K. Pritchard. *Toronto Sunnybrook Regional Cancer Centre, Division of Clinical Trials and Epidemiology, Toronto, Canada*

Women receive hormone replacement therapy (HRT) for relief of short term symptoms and long term effects related to menopause. Short to intermediate term effects include vasomotor reactions (hot flashes), while genitourinary symptoms such as dysurea, cystitis, dyspareunia and vaginal dryness, may occur in the short, intermediate and long term. Other short to intermediate term effects can include arthralgia, myalgia, fatigue, and mood and/or cognitive difficulties.