Conclusions: These data indicate that the triple combination is very active and safe in the primary treatment of the operable HER-2 positive breast cancer. A phase II study is ongoing.

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Implementation of adjuvant trastuzumab in breast cancer patients in the Netherlands

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Background: Recent studies have shown that trastuzumab combined with adjuvant chemotherapy improves outcome in women with HER2-positive breast cancer. Based on these results, a new national guideline was released in the Netherlands on September 15th 2005 stating that adjuvant chemotherapy should be combined with trastuzumab for women with HER2-positive breast cancer. This study evaluates the implementation of trastuzumab in clinical practice, guideline compliance and regional differences between the eight Comprehensive Cancer Centre regions in the Netherlands.

Methods: All women diagnosed with breast cancer between September 2005 and January 2007 were selected from the population based Netherlands Cancer Registry (NCR), covering all 16.4 million inhabitants. Women without surgery, with metastases at diagnosis or who received neoadjuvant chemotherapy were excluded. HER2 overexpression was recorded in the NCR based on IHC scores or FISH if indicated.

Results: The study included 14,934 patients. Of those, 1,928 (13%) had a tumour which overexpressed HER2. HER2 overexpression decreased with age from 22% in women under 40 years to 9% in women $\geqslant$70 years. Of all 1,928 women with HER2 overexpression, 1,114 (58%) received adjuvant chemotherapy. This percentage decreased from 93% among women <40 years to 8% among women 70−79 years of age. Of 1,585 women <70 years with HER2 overexpression, 1,095 women received adjuvant chemotherapy. Of these, 6% did not receive trastuzumab (regional range: 3−16%, p = 0.001). This percentage decreased from 9% in the first 4 months after release of the new guideline (regional variation 0−24%, p = 0.029) to 3% in the last trimester of 2006 (regional variation 0−12%, p = 0.517). Most common reasons for women not to receive trastuzumab were cardiotoxicity (29%) and patient refusal (21%). In 8% others reasons were given, in 42% no reason was given in the medical chart.

Conclusion: The percentage of women with HER2-positive breast cancer is markedly lower than the assumed 25% in the Netherlands. Of women with HER2 overexpression treated with adjuvant chemotherapy, 6% did not receive trastuzumab. The implementation of trastuzumab in clinical practice was rapid, with significant regional variation. One year after introduction in the guideline, regional differences disappeared. There was a known legitimate reason not to give trastuzumab in 58% of the 61 patients who did not receive trastuzumab.

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A validated analytical method for the simultaneous quantification of tamoxifen, endoxifen, anastrozole and letrozole

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Background: Liquid chromatography hyphenated to tandem mass spectrometry (LC/MS/MS) represents a powerful analytical method for the quantification of drugs in patients. Concerning the endocrine therapy of breast cancer, LC/MS/MS methods have been developed for therapeutic drug monitoring. However, none of the published methods allows for the simultaneous analysis of estrogene receptor antagonists as well as aromatase inhibitors. Thus, our aim was to develop and to validate a LC/MS/MS method covering drugs frequently prescribed in the endocrine therapy of breast cancer (tamoxifen, anastrozole, letrozole) allowing for a convenient pharmacokinetic drug monitoring.

Material and Methods: Blood plasma samples were collected from 320 patients undergoing endocrine breast cancer therapy and stored at −20ºC. To prepare a sample for LC-MS/MS analysis, 1 ml plasma was treated with a solid phase extraction procedure using a cation mixed-mode polymeric sorbent phase (Strata-X-C cartridges, Phenomenex, Torrance, CA). Chromatographic separation was accomplished on a reversed-phase column (200 mm $\times$ 0.5 mm, Eurosphere-C18, 5 μm, Knauer, Berlin) by using a gradient of acetone in an aqueous hexafluorobutyric acid solution. Mass spectrometric detection was performed on a quadrupole-quadrupole-linear ion trap instrument (Q Trap 3200, Applied Biosystems, Foster City, CA).

Results: We have developed a fully validated method for the simultaneous quantitative analysis of tamoxifen, its active metabolite endoxifen, and the non-steroidal aromatase inhibitors anastrozole and letrozole in human plasma. Validation was accomplished according to published guidelines [1] for a concentration range of 25–500 ng/ml for tamoxifen, 10–200 ng/ml for endoxifen, 5–200 ng/ml for anastrozol and 10–300 ng/ml for letrozol. The applicability of the method has been demonstrated by analyzing plasma samples of 320 patients treated with tamoxifen, anastrozole and letrozole.

Conclusion: The developed method represents a reliable and convenient tool for the simultaneous quantitative analysis of tamoxifen/endoxifen, anastrozol and letrozole allowing for convenient pharmacokinetic drug monitoring in the endocrine therapy of breast cancer.

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Adjuvant endocrine therapy in premenopausal women − toxicities and adherence rates from a tertiary care centre

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Background: Multiple randomized trials have demonstrated the efficacy of aromatase inhibitors (AIs) in postmenopausal women with hormone receptor positive (HR+) early-stage breast cancer (EBC). Ongoing clinical trials are examining the role of AIs given concurrently with ovarian suppression (OS) in premenopausal women with HR+ EBC. This study reports on toxicities and adherence rates observed in premenopausal women treated with OS and tamoxifen (Tam)/AIs in an academic cancer centre.

Material and Methods: Premenopausal women with HR+ EBC were identified through a home LHRH antagonist injection registry from Jan/05 to May/09. Data collected included: demographics, treatments, choices of endocrine therapies, treatment toxicities and adherence rates.

Results: 84 eligible patients (pts) were evaluated. Median age at diagnosis was 44 years (range: 24−53). Stage was I/II/III in 14/47/23 pts and 32 (38%) pts had her2/neu positive disease. Median BMI was 25.6. The majority of pts (90%) received chemotherapy. Initial endocrine therapy choices included Tam alone/AI+ OS/Tam+OS in 14/62/8 pts. Of the Tam alone group, 93% of pts switched to AI+OS and 7% switched to Tam+OS. The AI+OS group had 90% adherence rate at the time of evaluation. Few pts switched from AI+OS to Tam (1.6%) and Tam+OS (4.8%). Most pts (19/23) with stage III stage were on AI+OS. 79 pts had evaluations on BMD with 33 pts having follow-up BMD studies. 44% pts proceeded to have bilateral oophrectomy. Common toxicities for pts on AI+OS were arthralgia/myalgia (40%), hot flushes (35%), fatigue (19%), vaginal symptoms (18%), weight gain (15%), sleep disturbances (10%) and psychosocial issues (7%).

Conclusion: The use of AI+OS is not the current standard hormonal treatment in premenopausal women with HR+ EBC. In our experience, it is unclear if this choice has been driven by patient choice or physician advice. The 90% adherence rate in AI+OS group seems to be higher than the clinically observed AI adherence rates in postmenopausal women despite significant toxicities from treatment. Survivorship issues are complex in premenopausal woman and require careful attention and standardized approach.

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Actual or adjusted surface area: which should we use?

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Background: Calculation of chemotherapeutic drugs doses was standardized to Body Surface Area, with the aim to produce optimum systemic drug level & minimize drug toxicity; it also can be very challenging in obese cancer patients. Obesity represents a condition of excessive adipose tissue with its currently accepted definition is defined as Body Mass Index >30 kg/m^2); it once believed that obese patients who received chemotherapy on their actual body weight would result in increased toxicity, secondary to distribution of lipid soluble drugs into the adipose tissue. By using Adjusted Body Weight it's assumed that cancer patients would receive a dose of a particular cytotoxic drug associated with an acceptable degree of toxicity without reducing its therapeutic effect. The aim of this study is considering the use of adjusted body weight for calculation of chemotherapeutic drugs