context of progressive disease and, in one case, the pt had subsequently received an investigational anthracycline.

**Conclusion**: The addition of Herceptin to docetaxel significantly improved response rate, duration of response, time to progression and overall survival, with little exacerbation of toxicity.

**240** ORAL

**Intermittent/alternated therapy with tamoxifen and medroxyprogesterone acetate prolongs time to resistance to tamoxifen without benefit for (progression free) survival in patients with advanced breast cancer. Results of an EORTC phase III study (trial 10863)**

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**Introduction:** Patients with advanced breast- or prostate cancer, who relapse after stopping endocrine treatment during response may have repeated remissions when the same treatment is given again. In this study results of intermittent tamoxifen (T) or intermittent T alternated with medroxyprogesterone acetate (MPA) during response were evaluated.

**Patients and methods:** Postmenopausal patients with possible hormone responsive advanced breast cancer who had an objective remission or stable disease after 4 months of first line T therapy were randomised to continue T (40 mg daily) or to intermittent T (2 months break, two months treatment etc.) or intermittent/alternated T and MPA (300 mg daily). If progression occurred during break or during MPA, patients received T continuously. Endpoints of the study were proven resistance to T and (progression free) survival.

**Results:** As reported earlier [1], and after a median follow-up time of 8 years the median time to resistance to tamoxifen in 276 randomised patients were 12.2, 12.4 and 23.3 months for T, intermittent T and T/MPA respectively. The difference between T and T/MPA was statistically significant ($p<0.001$). After reinstitution of T in patients who relapsed during break or MPA, only 30% achieved stable disease. The median survival times did not differ significantly (36.1, 36.1 and 32.1 months respectively). Although data about subsequent therapy after resistance to tamoxifen are missing, it is plausible that a considerable number of patients from the T and intermittent T arms received MPA or another endocrine modality explaining that survival times in the tree arms were about equal.

**Conclusion:** It appears that the longer time to resistance to tamoxifen (or endocrine treatment in general?) in the T/MPA group but not in the intermittent T group is predominantly a consequence of the non cross resistant character of this modality and not of the intermittent administration of the therapy.

**References**

[1] L. Beex et al. Continuous vs. intermittent tamoxifen versus intermittent/alternated T and medroxyprogesterone acetate in advanced breast cancer. An EORTC phase III study. Breast Cancer Res Treat 2002; 76: S72. Abstr. 252.

**241** ORAL

**First results of a randomized phase III trial comparing exemestane versus tamoxifen as first-line hormone therapy (HT) for postmenopausal women with metastatic breast cancer (MBC) – EORTC 10951 in collaboration with the exemestane working group and NCIC Clinical Trials Group**

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**Introduction:** Over the last three decades, the antiestrogen Tamoxifen (T) remained the standard first-line HT in postmenopausal women with hormone-responsive MBC. Recent data from randomized phase III trials indicated however that third generation non steroidal aromatase inhibitors (AI) like Anastrazole and Letrozole may be as efficient, or even more active, with a different toxicity profile, than Tamoxifen. Exemestane (E) is another third generation AI, which is in fact the sole displaying a steroidal structure. Interestingly, it permanently inactivates the aromatase and is devoid of total cross-resistance with NSAI. Because of this, and in view of its demonstrated activity against MBC progressing after 1st- or 2nd-line HT, the EORTC Breast Group initiated in 1996 a randomized phase II–III clinical trial aiming at comparing the efficacy and safety of E versus T.

**Methods:** Patients with measurable disease were eligible if they had received no prior hormone therapy for MBC and had either an hormone receptor positive status, or an unknown status with a long disease-free interval. They were randomized to T 20 mg/day or E 25 mg/day in this open-label study. The primary endpoints of the phase II and III were respectively activity (Response Rate – RR) and efficacy (Progression Free Survival – PFS). The phase III trial aimed at identifying a median PFS increase of 3 months (i.e. from 7 to 10 month) in favor of E. Safety was a secondary endpoint for each step.

**Results:** Between 10/1996 and 07/2002, 382 patients were randomized by 81 institutions from 25 different countries. The results of the initial phase II part of the study, which accrued 122 patients, showed a promising overall RR, clinical benefit rate and response duration in favor of E. The incidence of serious toxicity was low and E was well tolerated; moreover, no adverse effects on the lipid profile were observed, at variance with observations made on NSAI. All conditions were fulfilled to continue with a randomized phase III trial (Paridaens et al., Ann. Oncol, 14, 1391–8, 2003). Presently, 284 (74%) patients have either progressed or died.

**Conclusions:** The number of events needed to perform the primary efficacy analysis has recently been reached and the data base is in its final stage of cleaning. A full (efficacy and safety) report of the results of this trial will be presented at the meeting.

**242** POSTER HIGHLIGHT

**Staging in patients with locoregionally recurrent breast cancer: current practice and perspectives for PET**

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**Background:** At least 20% of patients with locoregionally recurrent (LRR) breast cancer develop distant metastases within 18 months after diagnosis and salvage treatment of the recurrence. The yield of the current staging procedures among asymptomatic patients with an early stage of primary breast cancer is low. Since 1997 new diagnostic modalities such as 2-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) have emerged with promising results as a highly sensitive and accurate method for restaging patients with suspected breast cancer recurrence. However, one of the first steps in the assessment of new and expensive technology is to obtain adequate knowledge of the efficiency of current clinical practice without the new test.

**Objective:** The aim was to obtain representative data on the extent and yield of daily clinical practice when staging patients with a LRR of breast carcinoma and to discuss the perspectives for PET.

**Methods:** We used the population-based Eindhoven Cancer Registry to select all breast cancer patients in the southeast of the Netherlands with a first episode of LRR between January 1, 1994 and June 30, 2000. Additional data were collected from medical records at the departments of surgery and internal medicine. Furthermore, we asked all physicians responsible for treatment of LRR about their opinions on staging procedures and actual treatment policy.

**Results:** Medical records showed that clinicians used a relatively homogeneous set of routinely applied screening tests, which was confirmed by the outcome of the questionnaire. At LRR presentation, 16% of patients were found to have distant metastases. Patients with diagnosed distant metastases were less likely to undergo locoregional surgery and more often received systemic treatment than patients without distant metastases after staging. Within 18 months, an additional 24% of the patients proved to have clinically overt distant metastases. The questionnaire revealed that 44% of clinicians were not satisfied with the yield of the conventional imaging techniques; 33% indicated that the sensitivity was too low.

**Conclusion:** Current staging procedures detected only 40% of distant metastases in patients with LRR breast cancer (based on 18 months of follow-up). This result is in accordance with the opinion of many clinicians who were not satisfied with the yield of conventional imaging techniques and warrants a study of more sensitive imaging techniques such as PET.