pCHT was performed. The interphase cells were marked with the antibody 2E11 (against the tumor-associated antigen TAG12).

Results: The rate of TCD were unchanged before and after pCHT (52.3%; n = 22). In only 4 patients the finding changed (2 from positive in negative and 2 viceversa). In the matched pair analysis there were tumor cells in the bone marrow in 51.7% of the cases (n = 90) after pCHT; and in 49.4% (n = 86) in the control group without pCHT. Distant metastases were diagnosed in 27 patients (24 TCD positive; 3 TCD negative, $p < 0.001$) in the study group.

Conclusion: Our results show that a reduction of tumor size by NACT is possible, but no suppression of tumor cell shedding. Moreover, it is unclear whether the NACT has an effect on the metastatic potential.

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Short term *vs* lifelong adjuvant tamoxifen in early breast cancer (EBC): A randomized trial (TAM-01)

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In 1986, a multicentric randomised trial was initiated to compare a lifelong adjuvant TAM to a short term adjuvant TAM. Were eligible patients with EBC receiving adjuvant TAM since 2–3 years, disease-free since primary treatment, aged 75 years or younger. From 9/1986 to 5/1995, 3793 patients were randomized; 1882 (49.6%) patients stopped TAM (control) while 1911 (50.4%) patients continued TAM (lifelong) at the same dose than previously prescribed, until recurrence or death. Data was updated 11/1996; an intent to treat analysis was performed. Main prognostic factors (age, tumor size, nodes involvement, hormonal receptors) and initial treatment were well balanced and mean TAM duration at randomisation was 28 months in each group. The mean follow up time is 54 months. Overall, 318 and 258 patients have relapsed in the control group and lifelong group, respectively, leading to a 5-year disease-free survival (DFS) rate of 76% and 82%, and a 7-year DFS rate of 71% and 77% ($p = 0.0025$). In contrast, overall survival (OS) does not differ between the two arms, with 86% and 85% 5-year OS rates, and 79% and 78% 7-year OS rates, respectively ($p = 0.49$). We conclude that although no survival advantage is noted, patients do benefit from longer TAM with significantly better DFS. Long term follow up is needed to (1) assess these results, (2) appreciate the decrease in incidence of controlateral BC, and (3) estimate the treatment-associated second cancer risk.

Supported by a grant from ZENECA Pharma, France.

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The effect of oral clodronate on bone mineral density in women with primary breast cancer

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We have undertaken a double blind randomised two centre trial (RMH and TBCC) to evaluate bone mineral density (BMD) in over 300 patients with primary breast cancer given clodronate 1600 mg/day po (clod) or placebo (plac) for 2 years. Patients were accrued, randomised and received appropriate primary surgical, and medical treatment (chemotherapy and tamoxifen) and have completed follow up for at least 2 years without metastatic relapse. (RMH 103 clod, 93 plac, TBCC 53 clod, 62 plac). The median age, height, weight, menopausal status and type of primary surgical, adjuvant or neoadjuvant medical treatment were well matched for both treatment groups. BMD in the lumbar spine and hip were measured using dual energy xray absorptiometry (Hologic densitometer) at the start of clod/plac and after one and two years of treatment and calculated as % change of the initial treatment reading. The clod group had a small mean gain of 0.18% compared to the plac group which had a mean loss in spinal BMD of 2.2% (Treatment effect +2.38%, CI 1.36, 3.41 $p < 0.001$). Similarly the clod group had a mean gain of 0.40% in hip BMD compared to a mean loss of 0.34% in the clod group (Treatment effect +0.74%, CI −0.13, 1.6 p = NS). After 2 years the treatment effect for clod in spinal BMD was +1.73% (CI 0.12, 3.34 $p < 0.05$) and hip BMD +1.85% (CI 0.51, 3.20 $p < 0.01$). All subgroups of menopausal status and type of adjuvant/neoadjuvant medical treatment appeared to gain benefit. In patients who receive cancer treatment for primary breast cancer, these results indicate that use of oral clodronate will significantly reduce the loss of BMD.

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Randomized multicentric study of perioperative chemotherapy with mitoxantrone (MTZ) in early breast cancer

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Purpose: The aim of this multicentric randomized trial was to determine whether perioperative chemotherapy (POC) could change early breast cancer course.

Methods: A total of 578 women with early breast cancer (stage I to IIIA) were randomized to compare surgery followed by one course of POC (MTZ 14 mg/m^2) versus surgery alone. Premenopausal women with positive axillary nodes or negative hormonal receptors and grade 3 received adjuvant chemotherapy (fluorouracil, MTZ, cyclophosphamide) for 6 months. Menopausal women received tamoxifen.

Results: 554 patients were evaluable (192 premenopausal, 362 menopausal). Toxicity was acceptable: no infection, no cardiac event. Disease-free survival (DFS) and overall survival (OS) were not significantly prolonged in the chemotherapy arm. The interim analysis at 23 months median follow up in 1992 showed a significant benefit for the POC arm in term of metastase free survival (MFS) ($p = 0.02$, $\alpha = 0.05$). At final analysis at 7.4 years median follow up, in 1996, there was a trend towards improvement of MFS in the POC regimen ($p = 0.047$, $\alpha = 0.02$).

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Adjuvant radiotherapy in breast cancer and risk of ischaemic heart disease

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Purpose: To assess the occurrence of ischaemic heart disease (IHD) after breast cancer radiotherapy in long-term survivors.

Methods: In the years 1982 to 1989, 321 high-risk breast cancer patients from the county of Aarhus were included in the DBCG protocol 82 and randomised to post-mastectomy irradiation plus systemic treatment or systemic treatment alone. The chest wall was irradiated with 2 anterior shaped electron fields. Chest wall thickness was measured with ultrasound and electron energy chosen to include the clinical target volume in the 85% isodose. The target depth for the internal mammary nodes was chest wall thickness plus 0.5 cm and chest wall thickness minus 1 cm for the scar region. The median absorbed dose was 50 Gy in 25 fractions with 5 f/w. The median follow-up time was 8.3 years.

Ninety-five out of 122 survivors of this study group agreed to participate in a prospective study evaluating late morbidity including cardiac anamnesis, clinical examination, ECG and chest radiography. All left-sided breast cancer patients were offered a myocardial perfusion scintigraphy and 16 patients agreed. Only the result of this part of the study will be reported here. Sestamibi-SPECT scannings were performed as a rest/dipyridamole 2-day protocol. Scintigrams were blindly evaluated using a 5-point scale in a 20-segment model of the left ventricle.

Results: There was no difference between the scintigrafic findings in the two groups. Four of 9 study group patients, and 4 of 7 controls had significant defects on scintigraphy, indicating IHD. Only one patient showed an anterior defect, and this patient was a control patient. None of the patients had symptoms of IHD.

Distribution of scintigraphic defects:	Radiotherapy	Control
Reversible	2	1
Partly Reversible	1	1
Irreversible	1	2

Conclusion: Our scintigraphic data do not support any increased risk of IHD among survivors of breast cancer treated with optimal radiation technique.