**Friday, 2 October 1998** **09:30-11:30**

**JOINT SYMPOSIUM**

# Adjuvant therapy – state of the art, expectations and future directions

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## Adjuvant therapy: patient issues

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Abstract not received.

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## Facts and figures from the meta-analyses in breast cancer

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The current cycle of the 5-yearly worldwide meta-analyses in early breast cancer has brought together information on 130,000 randomised women, with a median follow-up of about 10 years. 40,000 were in trials of adjuvant hormonal therapies (3000 ovarian ablation; 37,000 tamoxifen), 50,000 were in trials of chemotherapy (10,000 monochemotherapy; 20,000 polychemotherapy vs not; 20,000 one polychemotherapy versus another), and over 30,000 were in trials of local therapy (including 20,000 in trials of radiotherapy). These trials did not generally involve women with good-prognosis screen-detected tumours, among whom any benefits might well be smaller.

For women with receptor-positive disease, or for women whose receptor status has not been determined, tamoxifen is of substantial benefit both in those aged under 50 and in older women: 5 years of adjuvant tamoxifen appears better than 2 years, but there is as yet inadequate evidence as to whether 10 years of tamoxifen is better than 5. In such women tamoxifen produces a decrease in breast cancer mortality that is about 50 times the increase it produces in endometrial cancer mortality, and, in more than 200,000 woman-years of randomised experience, tamoxifen had no apparent effect on mortality from causes other than breast or endometrial cancer. In terms of the 10-year incidence of new tumours, the extra number of endometrial cancers that it caused is smaller than the number of new cancers it prevented in the opposite breast.

Polychemotherapy (e.g. with some months of CMF or of an anthracycline-based regimen) is of substantial value for women aged under 50 and is of some value for women aged 50–69, but has hardly been tested in women aged 70 or more.

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## Adjuvant systemic treatment for operable breast cancer – Standard therapies and new approaches

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AST reduces relapses and prolongs survival of women with operable breast cancer. This is true for all studied subpopulations (i.e., N+ and N– disease, pre- and post-menopausal ages). Primary chemotherapy has shown an effect in controlling systemic disease similar to the one obtained with postoperative chemotherapy of the same type. The overall effect of the adjuvant systemic therapies is modest but clinically and humanly relevant. Adjuvant endocrine therapies include tamoxifen and, for premenopausal patients, ovarian ablation. Adjuvant chemotherapy regimens mainly include CMF or anthracycline-containing regimens, or the sequential use of both. In postmenopausal women, the use of the two modalities (endocrine and cytotoxic) together has proven to be more beneficial than each modality alone, but optimal combinations are still in trial. In premenopausal patients, especially those with tumors classified as ER+, the combination of ovarian function ablation, tamoxifen, and chemotherapy is likely to yield better results than each modality alone. However, the best way to combine these treatments is still unknown. Examples for issues under current investigation are:

(a) Novel chemotherapies (e.g., taxanes) and endocrine therapies (e.g., GnRH analogs, use of aromatase inhibitors)
(b) High-dose chemotherapy with marrow support
(c) Integrating pre- and postoperative systemic treatments

The selection of adjuvant systemic therapies outside trials include:

(a) Determination of risk of relapse
(b) Extrapolating relevant data from results of clinical trials
(c) Integrating patient's preference with physician's "best bet"

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## BIG – The breast intergroup

Martine J. Piccart. *On behalf of "BIG"; Institut Jules Bordet, Rue Héger-Bordet 1, B-1000 Brussels, Belgium*

It has taken the oncology community 25 years to dissect the positive impact of adjuvant hormonal therapy and chemotherapy on the outcome of the breast cancer patient.

From this past experience in the field of adjuvant breast cancer clinical research, we have learned 1) that treatment effects are essentially modest, 2) that breast cancer is a complex and very heterogenous disease, 3) that in view of 1 and 2, *large* and well designed clinical trials are needed.

Innovative strategies for conducting clinical trials of breast cancer adjuvant therapy are becoming a necessity if we want to accelerate progress in this field but also in view of a) an *explosion* in new forms of anti-cancer therapy, such as anti-signal transduction or anti-angiogenesis agents, which could each contribute some improvement if optimally integrated into existing treatment regimens, b) growing difficulties in finding support for trials not investigating "drug" questions (for example surgical or radiotherapy trials), c) increasing awareness that scientific independence from the Pharmaceutical Industry needs to be maintained.

BIG is a newly formed Intergroup covering Europe-Australia and New Zealand, which was set up as a possible answer to a + b + c. Its current clinical research program will be presented.

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## The place of modern radiotherapy in loco-regional control and long-term survival in breast cancer

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**Introduction:** There is a large spectrum of breast cancers (BC) ranging from in-situ to inflammatory tumors and a debate continues between the supporters of BC as a "local disease" and others who consider BC almost always as a "disseminated" disease. In fact, the truth is beetween the two and both positions are compatible.

**Breast irradiation after lumpectomy:** For DCIS, the updated results of the NSABP-B17 trial confirm the benefit of breast irradiation (50 Gy) with a reduction of local recurrences (LR) from 26.8% to 11.2%. In a retrospective study by the French Cancer Centers, we found similar results (25.6% vs 13.3%). For invasive lesions, five randomised trials confirm an extremely high reduction of LR rates by irradiation, but only with a slight increase in survival. Thus, until now, no criteria exist to avoid radiotherapy after limited surgery.

**Chest-wall irradiation after mastectomy:** In case of risk factors (T3 T4, pN+, presence of diffuse vascular invasion), chest wall irradiation significantly reduces the LR rates, both in women and men.

**Nodal irradiation:** In case of the risk factors cited above nodal irradiation (50 Gy) reduces regional recurrences (RR) from 15–35% to 7–10%. Recently, two randomized trials confirm a significant reduction (32% vs 9% and 23.4% vs 11.6%) of LR and RR by irradiation even when CMF chemotherapy is used. Moreover, an important advantage in the 10 year survival rates is also demonstrated (54% vs 45% and 62% vs 53%). However these results are possible only by an optimal radiotherapy technique. The most important point is the mandatory use of a "mixed" and "alternate" beam (with at least 60% of delivered dose by electrons) to treat internal mammary nodes, avoiding the heart.

**Conclusion:** Modern radiotherapy is essential in the locoregional control of BC, both in early and advanced disease. In the later case, an optimal combination with chemotherapy is necessary.