Inhibitor in N– breast cancers defines 3 distinct risk populations. Besides differentiating populations with different outcomes, some prognostic factors assist therapy decisions: in NSABP B14 trial, the outcome of good prognosis patients (ER+) was improved by tamoxifen. Over-expression of c-erb B-2 also seems associated with chemotherapy resistance.

SY-5-2 Selection of Treatment

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To date the qualitative values of estrogen (E) and progesterone receptors (PgR) as well as their classification into "positive" or "negative" are the most helpful values available in choosing between chemotherapy and a hormonal approach as adjuvant therapy for low risk patients. Age is also a factor, perhaps because more older women have higher ER and PR values. One possible treatment approach is shown below.

Patient Group	Risk		
	Minimal/Low	Moderate	High
Premenopausal			
ER positive	no treatment	tamoxifen	chemotherapy*
ER negative	–	–	chemotherapy*
Postmenopausal			
ER positive	no treatment	tamoxifen	tamoxifen
ER negative	–	–	chemotherapy*

* If chemotherapy refused, tamoxifen may be offered

Of course, for women in whom endocrine and chemotherapy may be equally efficacious, endocrine therapy is almost always to be preferred because it is less toxic. New data from clinical trials however may describe more patient groups in whom both endocrine and chemotherapy may be useful as has been the case for node positive disease.

SY-5-3 Results of the 1995 Meta Analysis

R. Gray. *UK*

Abstract not available.

SY-5-4 Trials in Progress and Trials Now Needed

H.J. Senn. *Switzerland*

Abstract not available.

SY-6. Postmenopausal Breast Cancer (September 12)

SY-6-1 Treatment of Operable Breast Cancer in the Elderly

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In Europe more than one third of patients with breast cancer are aged over 70 and the disease is equally aggressive in older and younger women. Because of increasing life expectancy more cases will be elderly and more will live long enough to develop relapse if treated suboptimally.

Results from clinical trials suggest tamoxifen alone is inadequate primary treatment with a substantial proportion of cases developing progression and relapse. Wide local excision and tamoxifen appear to be as equally effective as a mastectomy in terms of mortality rate. Studies need to be conducted to identify which patients can be treated safely by wide local excision and tamoxifen and others who require more aggressive local treatment such as mastectomy or radiotherapy.

SY-6-2 Place of Adjuvant Chemotherapy after 50

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Adjuvant chemotherapy has been considered as less effective after 50 than before in the first randomized trials. This was explained by Bonadonna as related to a worse compliance to treatment and a lesser dose intensity. The use of anthracyclines did not improved the results (Oncofrance, NSABP–B12). However, the first overview by Peto found out a trend in the reduction of odd ratio death (9% ± 9). In the second metaanalysis, a benefit was observed in the annual death rate (13% ± 4) but with a less extend than for premenopausal patients (24% ± 5).

Similarly, the annual rate of relapse was reduced by 24% (± 3) instead of 36% (± 5) in the premenopausal setting.

It seems evident that this benefit was related also to age. In the 50–59 group, the improvement in the odd ratio relapse was the same (25%) whatever was the menopausal status, but survival was still better for premenopausal patients (13% vs 23%). Between 60 an 69 years old, the benefit was significant for relapses. Unfortunately, the magnitude of trials was too poor to give any judgment after 70.

The combination of chemotherapy and Tamoxifen was superior to chemotherapy alone (–28% relapse; –20% deaths), but better only for relapses when the combination was compared to Tam alone. Conclusions were the same for the negative and positive node groups. Individual trials were not really convincing but the most large ones had the same trend that the meta-analyses (B09, B16, Ludwig III). Major questions are still unsolved: what is the best combination of drugs? Are anthracyclins more toxic after 50?

Is the small absolute benefit of 12% at 10 years justified in view of the not optimal quality of life? Is there a place for chemotherapy after 70?

Finally, the importance of hormonal receptors status has not been clearly determined for the choice in the best treatment for menopausal patients.

SY-6-3 Skeletal Problems in Postmenopausal Women

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Natural menopause as loss of ovarian function determines acceleration in bone remodeling and subsequent loss of skeletal mass. The outcome is an increase risk of fractures specially in spine, hip and forearm. Highly reproducible measurement of bone mass is now available using single or dual photon or x-ray absorptiometry, quantitative computed tomography or ultrasound. A low bone mass and an accelerated rate of bone loss are predictive of fracture risk and difformities due to microarchitectural abnormalities. Hormone replacement therapy (HRT) is clearly effective in the prevention and treatment of postmenopausal osteoporosis, however, other treatments are also effective and should be used when HRT is contraindicated. In postmenopausal patients, long-term adjuvant Tamoxifen has been shown to protect bone mineral density of low-risk breast cancer patients; a similar effect was observed in patients receiving Tamoxifen in a prevention trial. Non hormonal treatments as calcium, fluoride, calcitonins and various bisphosphonates are investigated in osteoporosis treatment or prevention.

SY-6-4 Hormone Replacement Therapy

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Replacement therapy (RT) with estrogen (E) or combinations of E and progesterone (P) has traditionally been contraindicated in women with a previous diagnosis of breast cancer. The rationale underlying this recommendation relates to observations from in vitro systems and animal models where, by and large, E is required to maintain breast cancer cell growth. The role of P varies in different in vitro models and animal systems, sometimes acting together with E to promote breast cancer growth and sometimes retarding it. Other pertinent observations include epidemiologic studies of the role of E and E plus P in the etiology of breast cancer. Only a weak relationship between E and the development of breast cancer has been demonstrated, the role of P remains unclear, and it is only with long term use of E (≥ 15 years) that a clear increase in risk of breast cancer development can be consistently demonstrated. With this background and with the diagnosis of a large number of very early breast cancers as a result of screening programs, the dogma that E should not be given with any previous diagnosis of breast cancer is being reexamined. There is limited data examining the role of ERT in women with a previous diagnosis of breast cancer. One can infer however from data about pregnancy following breast cancer and from a few small case series and 2 small case control studies in which E has been given to women with a previous diagnosis of breast cancer that estrogen in this setting may not be as dangerous as has been believed. One randomized study of ERT in this setting is ongoing. Additional data will be required before definitive recommendations regarding ERT in women with a previous diagnosis of breast cancer can be made.