Friday, 22 March 2002 **14:45–16:15**

SYMPOSIUM

The management of breast cancer in young women

318 INVITED

Genetic and histologic features of breast cancer in young women

M.J. Van de Vijver. *The Netherlands Cancer Institute, Amsterdam, The Netherlands*

Breast cancer occurs mainly in older women, but approximately 10% of breast cancer patients are younger than 40 years of age at diagnosis; and 20% are between 40 and 50 years of age. Not only is the diagnosis of breast cancer at such young age emotionally devastating, the characteristics of these tumors distinguish them from tumors which occur at older age. Most importantly, in young patients the risk of local recurrence after breast conserving treatment is greatly increased and overall survival is lower compared to older patients.

Although some studies have shown an association of younger age with risk factors for local recurrence (multicentricity, multifocality, vascular invasion, high tumor grade and extensive DCIS) in other studies age remains an independent risk factor. This indicates that in younger patients not yet identified risk factors must be present.

Since genetic alterations are the cause of cancer development, it is expected that the combination of specific genetic alterations in tumors is predictive of clinical behavior. However, until now, the use of genetic alterations as prognostic factors in breast cancer has been very limited and genetic alterations specifically associated with breast cancer at young age have not (yet) been identified.

In approximately 5-10% of breast cancer patients, a genetic predisposition to develop breast cancer is present. In approximately 5% of the cases, germline mutations in the BRCA1 and BRCA2 are identified. If a woman develops breast cancer at an age younger than 35 years, the chance that a BRCA1 or 2 mutation is present is approximately 15%; if breast cancer develops at an age younger than 40 years, this risk is approximately 10%. BRCA1 associated carcinomas frequently are of high grade and estrogen receptor negative.

Gene expression profiling using micro-array analysis offers a systematic method to perform extensive expression profiling within a tumor, and will reveal the state of many regulatory pathways that may be affected by genetic alterations in one single experiment.

Recently, we have identified a gene expression profile associated with high risk of distant metastasis in lymph node negative breast cancer patients younger than 55 years of age.

We are presently validating the prognostic value of this poor prognosis signature; in addition, we are investigating whether gene expression pattern can identify patients at high risk of developing local recurrence after breast conserving therapy.

319 INVITED

The management of breast cancer in pregnancy

A. Jones. *Royal Free Hospital, Department Clinical Oncology, London, UK*

Breast cancer is uncommon during pregnancy and lactation occurring in up to 3% of diagnosed cases. The prognosis depends on conventional prognostic factors and is not influenced by pregnancy per se; although this may lead to delay in diagnosis and hence higher stage. Termination is generally recommended in the first trimester but diagnosis in the second or third trimester warrants careful discussion. While radiotherapy is contraindicated throughout pregnancy, cytotoxic chemotherapy can be used from the second trimester onward safely with no adverse fatal or maternal outcome. The timing of delivery may be influenced by the use of chemotherapy and breastfeeding is contraindicated within 2 weeks of cytotoxic drug administration. Long term follow up of children with respect to their own fertility is indicated and long term side effects is needed.

320 INVITED

Is reduction of high local recurrence rate in young women possible?

H. Bartelink. *The Netherlands Cancer Institute, Radiotherapy Department, Amsterdam, The Netherlands*

The local recurrence rate after breast-conserving therapy is strongly correlated with age. Higher rates of local recurrences are seen in younger patients. This phenomenon was also observed in a trial of the EORTC, where 5569 patients were randomized after whole breast irradiation. They were randomized between additional radiation dose of 16 Gy and no dose to the site of the primary tumor. Factors associated with local recurrences were more often seen in young patients. To name a few important ones: smaller excision volume of the primary tumor, more frequent re-excision performed because of incomplete removal of the primary tumor and a higher malignancy grade. The multivariate analysis for prognostic factors and the treatment pointed out the two most important factors for local control: age and the additional radiation dose given. In patients 40 years of age and younger the 16Gy higher radiation dose was able to reduce the local recurrence rate with a factor 2.

To improve the local control rate in young breast cancer patients it is necessary to pay attention to each step of the treatment chain. It starts with precise information on the location of the primary tumor and its extension. New possibilities for delineating the borders of the tumor are becoming available with MRI and 3D ultrasound. These methods will assist the surgeon to completely excise the primary tumor at first attempt, and to guide the radiation oncologist to precisely deliver the additional radiation dose to the tumor bed. Adjuvant chemotherapy together with an additional radiation dose will also contribute to a better local control rate in young patients.

321 INVITED

Adjuvant systemic treatment for the very young (<35 years)

A. Goldhirsch[1], R. Gelber[2]. [1] *European Institute of Oncology, Milan, Italy;* [2] *Dana-Farber Cancer Institute, Boston, MA, USA*

Breast cancer rarely occurs in very young women. Only about 2% of the pts are 34 years old or less at diagnosis. Under 20 yrs the incidence is estimated to be 0.1 per 100,000 women, increasing to 1.4 for 20-24 yrs old, 8.1 for 25-29 yrs old, and 24.8 for 30-34 yrs old. Breast cancer at a young age has an unfavorable prognosis compared with the disease in older patients: higher grade, higher proliferating fraction, more vascular invasion and more N+ are observed. Some important issues, which relate to diagnosis and treatment of breast cancer at very young age include the desire to have children and concerns on side effects of endocrine therapies. Typically, young patients receive CT and in many countries clinicians are reluctant to employ ovarian ablation or other endocrine treatments. No adjuvant systemic therapy was given to young women with early stage breast cancer thought to have favorable prognostic factors in a large Danish study with 10,356 women less than 50 years old. The youngest, when compared with those >35 yrs had a significantly lower survival. No such trend was seen in patients who received adjuvant CT. Although the effect of chemotherapy for premenopausal patients is substantial, recent evidence on 2,233 patients treated with cytotoxics in IBCSG Trials suggested that very young women with endocrine responsive tumors had a significantly higher risk of relapse than older premenopausal patients with such tumors. In contrast, results for younger and older premenopausal patients were similar if their tumors were classified as endocrine non-responsive. Information from studies on 7,631 patients who were treated with CT alone in trials of three major US cooperative groups (NSABP, SWOG, ECOG) showed a similar interaction between the effect of age and steroid hormone receptor status of the primary tumor. This retrospective analysis on treatment outcome suggests that the endocrine effects of CT alone were insufficient for the younger age group (only about 30% of the patients stop menses from 12 - 6 courses of classical CMF). Additional endocrine therapies (tamoxifen or ovarian ablation or the combination of both) should be considered for these patients if their tumors express steroid hormone receptors. Such endocrine therapies might be the most effective component of their adjuvant treatment program.