

Thursday, 18 March 2004

08:30–09:15

EUROPA DONNA TEACHING LECTURE

Management of breast cancer in the elderly

213

INVITED

Management of breast cancer in the elderly

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Providing a good management of breast cancer for the elderly poses from many aspects important and difficult challenges. It is in many European countries already today a large quantitative problem with about 25% of all breast cancer patients being 75 years of age or older. Due to mainly demographic changes – and to a minor extent to an increase in risk – the problem will become larger in the near future with a rapidly increasing number of elderly with breast cancer up to 2020. Few national health plans have developed strategies to meet this challenge.

Despite common belief, breast cancer specific survival is not better in the elderly. On the contrary, several studies point towards a worse prognosis. The reasons for a worse breast cancer prognosis with increasing age are not clear. A more aggressive tumour biology, a less good host-defence towards malignant tumours, and diminished tolerance to treatments have been suggested as explanations. However, a low diagnostic and therapeutic activity have also been discussed as reasons; e.g. few women over 70 are offered screening. A debate is rising whether there are inappropriate selection mechanisms – such as low therapeutic activity based on age only rather than sound biological or clinical considerations – in play. One empirical underpinning to such a debate is that prognosis in breast cancer among elderly is different in different regions, even in regions geographically close to each other.

A clinical dilemma is that few trials have included women over 70. Very few have been specifically designed for elderly women. This is true for trials in primary treatment, adjuvant treatment and for treatment of recurrence – the latter being especially problematic given the worse prognosis discussed above. Thus, there is little empirical data to support rational clinical guidelines, leading to uncertainty about management of elderly and in the worst case contributing to age-biased treatment decisions. An important issue for clinical breast cancer doctors in Europe is to rapidly decide how we are going to meet these challenges.

Thursday, 18 March 2004

10:30–12:30

KEYNOTE SYMPOSIUM

The management of elderly women with breast cancer

214

INVITED

The local treatment of elderly women with breast cancer

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Local treatment of breast carcinoma in elderly women is becoming an important issue. The expansion of life-span, especially in women, is at the root of the increasing number of women over 70 that need a treatment of their breast carcinoma, a disease which is very common in old ages.

The main problem is that, for this group of patients, widely accepted guidelines are difficult to be formalized because the large number of variables make each case different from the others.

The main advantages of the management of breast cancer in old ages are: first that mammography regularly performed is very effective and may detect very small lesions, and secondly that the cancer cells are endocrine-dependent in a very high percentage of cases.

The main disadvantages are psychological in nature. In fact, very often the disease in old ages is accepted with fatalism and resignation. The motivations to resist and to fight the cancer are much weaker than in earlier ages. Also mutilations are badly accepted. Mastectomy is surprisingly difficult because an old woman sees this mutilation as "the beginning of the end" and as a first step to the final physical disintegration.

215

INVITED

The adjuvant treatment of elderly women with breast cancer

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Breast cancer is the most frequently diagnosed cancer in women living in industrial countries. Almost 50% of women who are diagnosed with breast cancer are >65 years old. Despite that, very few older patients have been included in clinical trials of adjuvant therapies, and few trials have been designed specifically to answer questions related to therapies for older women. One of two such trials designed and conducted during the late seventies was the IBCSG (formerly Ludwig Breast Cancer Group) Trial IV. Patients aged 66 to 80 were randomized to a tamoxifen-based endocrine therapy for one year or no further therapy after surgery for node-positive breast cancer. After 21 years median follow-up, patients who received the adjuvant treatment program had an approximately 30% reduction of chance of relapse. Disease-free and overall survival were both significantly in favor of the treatment group ($p=0.003$ and 0.05 , respectively) despite the large proportion of patients who died without relapse (due to competing causes of mortality in old age).

Once diagnosis, surgical treatment and pathological characterization of the disease are concluded, adjuvant decision-making algorithms include:

- Estimation of risk of relapse;
- Estimation of potential endocrine responsiveness;
- Extrapolation from results of previous clinical trials conducted in populations similar to that of the individual patient and her disease characteristics (usually in younger postmenopausal women)
- Evaluation of co-morbid conditions on life;
- Assessment of patient preferences and age-related concerns, of the patient, family and care-providing team.

Progress may be made through clinical trials which answer the following questions:

- Are there easily-manageable but effective chemotherapy regimens to offer to elderly patients with endocrine non-responsive disease?
- Should chemotherapy be prescribed to women with endocrine responsive disease and at high risk of relapse?
- Are there endocrine therapies which are more suitable for elderly women than tamoxifen given for 5 years?

The tendency to extrapolate information from experience in younger patients on one hand, and to neglect offering adjuvant therapies due to older age on the other, could be avoided if specific information is obtained for elderly women with breast cancer through clinical trials.

216

INVITED

Systemic treatments for metastatic disease in elderly women: cost–benefit considerations

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The systemic management of breast cancer in older women involves four setting: chemoprevention, neo-adjuvant and adjuvant treatment, and management of metastatic disease. A number of clinical trials have demonstrated that systemic treatment with tamoxifen "in lieu" of local treatment resulted in shorter freedom from progression and reduced overall survival in women aged 70 and older, and this practice has been all but abandoned. As chemoprevention has not produced yet a reduction in breast cancer-related mortality, this strategy should be considered experimental in older women. In the following discussion we will collapse together neo-adjuvant and adjuvant treatment that have similar implications in terms of cost benefits.

Adjuvant hormonal treatment of breast cancer has reduced recurrence rate and mortality to comparable rates in women under 60 and over 70, while the benefits of adjuvant chemotherapy seem to fade with age. At least two explanations, inability to administer full dose of chemotherapy and more indolent tumors, may account for the declining benefit of adjuvant chemotherapy with the patient age. Adjuvant chemotherapy appears a reasonable option for women with hormone-receptor poor tumors, and for those with lymph node involvement, especially in the presence of HER2/neu rich tumors. Patient selection should involve estimate of life-expectancy and of tolerance of treatment, while hemopoietic support with filgrastim or pegfilgrastim may allow the administration of full doses of drugs.

Management of metastatic disease involves hormonal treatment with aromatase inhibitors, Selective Estrogen Receptor Modulators (SERMs) and progestins in patients with hormone-receptor rich tumors, while the use of high dose estrogens and of androgens has been abandoned in the majority of cases. Aromatase inhibitors and the pure estrogen antagonist faslodex appear active even in HER2/neu rich tumors. Chemotherapy