Do Perspectives Exist for Further Improvements in Adjuvant Therapy of Early Breast Cancer?

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The question – and the question mark – set forth by the editors of this journal in the title of this invited commentary demonstrate a somewhat inpatient attitude, shared by many physicians, health care professionals, politicians and patient advocates today! Why does progress happen so slowly? Nevertheless -after many decades of frustrating stagnation of long-term survival expectations in early, operable breast cancer, treated only with surgery and loco-regional radiotherapy – adjuvant systemic therapies (chemo- as well as endocrine treatments) have clearly demonstrated a significant disease-free as well as overall survival benefit in virtually all stages of operable breast cancer during the past 10-15 years. This beneficial evolution has been extensively amplified by the Worldwide Oxford Overview and the Expert Consensus Panel at the 4th International Conference on Adjuvant Therapy of Primary Breast Cancer in St. Gallen in 1992 [1, 2]. What has happened since then?

During the past 3 years, several new concepts and treatment strategies have emerged and have been studied in various major breast cancer groups and treatment centers worldwide. Some of these can already be considered to assist in the primary treatment of operable breast cancer today, while others are still undergoing clinical trials for better definition of their practical usefulness. Most of these (research) problems were recently discussed during the 5th International Conference on Adjuvant Therapy of Primary Breast Cancer in St. Gallen, Switzerland in early March 1995, attended by more than 1,000 breast cancer specialists from 52 countries worldwide [3]. These evolutions include:

-Isolation of 'breast cancer genes' (BRCA 1-4), which will present new challenges in ongoing and future trials of chemo-prevention of breast cancer! -Biological diagnostics and therapies, involving particularly growth factors and angiogenesis, still to enter solid clinical trials, to demonstrate their usefulness in the adjuvant setting. -New factors for prediction of treatment response, such as c-ErbB2 and Ki67 expression for prediction of response to anthracycline-containing adjuvant therapies and resistance to tamoxifen or CMF: Results are interesting, but need to be confirmed in well-designed, randomized clinical trials.

The unsolved problems of concomitant or sequential adjuvant chemo-endocrine therapies [4], presently studied in various trials by the International Breast Cancer Study Group, and others. The concept of the prognostic impact of 'full-dose' chemotherapy: Based on (scarce) prospective trial evidence, dose reductions of more than 25% are highly detrimental in terms of adjuvant, curative treatment results [5]. This could greatly influence patient care and breast cancer mortality outside of trials, regarding the fact that 80-90% of patients in most areas are not treated

in prospective studies. The use of hemato-poietic growth factors has not even been systematically analysed in this regard.

The problem of really 'high-dose' chemotherapy with auto-logous bone marrow or peripheral blood progenitor cell support is a promising approach for better long-term survival benefit in patients at high risk of relapse, e.g. those with more than 4 (or at least more than 10) tumor-positive axillary nodes: More prospective trials to define the choice of treatment, clinical effectiveness and cost-benefit ratios are badly needed.

The definition of the importance and usefulness of new, very active single drugs such as taxanes in prospective trials in the adjuvant setting is highly important, regarding their complete-remission-induction potential (especially, if combined with anthracyclines) in advanced disease, but also regarding their high toxicity and their exorbitant costs.

Do any perspectives exist for further studies to improve adjuvant therapy of primary breast cancer? I am inclined to clearly write: yes!

It seems to me that there are more pertinent questions related to the improvement of adjuvant systemic therapy in breast cancer than interested and logistically able study groups available, to resolve these question marks in the near future!

However, in planning new adjuvant trials it would be extremely helpful if existing (national and international) breast cancer groups and working parties would not only be 'working', but rather would internationally work together in designing and executing common scientifically innovative and clinically relevant studies, which could be terminated within acceptable time intervals.

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3) The implementation of the concept of 'full-dose' chemotherapy outside of clinical trials could mark a major step forward in curative treatment of early breast cancer, translating clinical research data into clinical and epidemiologic experience. Although the present curative treatment effects of adjuvant systemic therapies in breast cancer are yet modest, they are real and give rise to hope of further improving long-term disease control, especially in younger patients with higher than average risk of recurrence. This bundle of hope and problems is discussed elsewhere in this journal and in other related international journals [3].

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