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Notes from the 8th St. Gallen International Consensus Conference on Primary Therapy of Early Breast Cancer

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This year, between 12-15 March 2003, 8th St. Gallen Consensus Conference was held in St. Gallen, Switzerland with more than 2500 participants from different countries. There were 56 participants from Turkey. In the last years, name of the conference was 'Adjuvant Therapy of Early Breast Cancer'. This year name had been changed as 'Primary Therapy of Early Breast Cancer'.

Professor Hans-Jörg Senn from St. Gallen, Switzerland, one of the chairpersons of the conference, pointed out that in earlier years 3 or even 4 years intervals were sufficient to justify conference repetitions, but the needs have clearly changed during recent years because of the rapidly growing and accelerated data about treatment strategies, diagnostic methods, genetics, therapeutic targets, etc. Biannual conference repetitions are now needed. European Breast Cancer Conferences will continue in alternative years to the St. Gallen conferences.

Opening address was made by Professor Umberto Veronesi from Milano, Italy. He said that in the last 10 years a number of revolutions had occurred in the biology of breast carcinoma and had deeply influenced our approaches to the disease in terms of prevention, detection and treatment. We learned the importance of quality of life. *Maximum tolerated treatment* changed to the *minimum effective treatment*. This new trends has led to limited surgery (instead of mutilating operations), more targeted radiotherapy (instead of large field involving the regional nodes), less aggressive chemotherapy (instead of high dose approach). This new trend will motivate more women to participate in early detection programmes.

Dr. Nancy Davidson from U.S.A. talked about the new data on endocrine treatments: New data over the last 2 years have begun to change tamoxifen primacy in the treatment of postmenopausal hormone receptor

positive breast carcinoma. Third generation aromatase inhibitors (anastrozole, letrozole and exemestane) are effective and safe drugs in postmenopausal patients with metastatic disease. In addition, in the adjuvant setting, the ATAC trial has shown that use of anastrozole is associated with reduced breast cancer events compared with tamoxifen after about 47 months follow-up, and a favorable toxicity profile has been observed to date except for increased fracture risk in the anastrozole arm. Combined use of anastrozole and tamoxifen does not offer any advantage over use of tamoxifen alone. Other trials also tested the role of other aromatase inhibitors as well as sequences of tamoxifen and aromatase inhibitors. For premenopausal women the role of ovarian ablation/suppression is of increasing interest. Goserelin with or without tamoxifen may be an alternative adjuvant therapy to classic CMF chemotherapy for hormone receptor positive premenopausal patients according to the results of ZEBRA, ABCSG 5 and IBCSG VIII trials. The role of ovarian ablation/suppression will be evaluated further in three (SOFT, TEXT and PERCHE) international trials.

Dr. Kent Osborne from USA, talked about the molecular mechanisms of hormonal resistance in breast cancer: Growth of breast cancer is regulated by a complex coordinated effort between estrogen receptor and growth factor signaling pathways. In the laboratory, overexpression of estrogen receptor coactivators such as SRC3 (AIB1) increases the agonist activity of estrogen receptor bound by SERMs such as tamoxifen. In an experimental model AIB1 and HER-2 account for de novo resistance to tamoxifen, which under these circumstances stimulates rather than inhibits tumor growth. This cross-talk between estrogen receptor and growth factor pathways also explains acquired resistance to tamoxifen in preclinical models. Interruption of these growth factors signaling pathways disrupts the cross-talk, and restores tumor growth inhibition with tamoxifen. These results are now being tested in clinical trials.

Dr. Martine J. Piccard from Jules Bordet Institute Brussels, Belgium, outlined the new data on breast cancer chemotherapy in the adjuvant setting: She mentioned about the 3 markers, and two prospective studies: First of them was UPA and PAI-1, two molecular markers of invasion already known for their powerful prognostic value in node negative (NN) breast cancer, seem to predict for enhanced benefit from adjuvant chemotherapy, while the benefit from adjuvant endocrine therapy seems independent of them. But their evaluation through a cytosolic assay is compromised for less than 1 cm tumors. The second data was related to identification of molecular signatures of breast cancer through microarray technology. These seem to be better predictors of clinical outcome in women younger than 55 years old with stage I and II breast cancer when compared to the currently used criteriae. These data need to be independently confirmed on larger sets of patients. Third marker was cycline-E. This data also needs confirmation in large prospective trials.

Dr. Piccard outlined the CALGB9741 study: Dose-dense versus conventionally scheduled (2 weeks versus 3 weeks intervals) and sequential versus concurrent combination chemotherapy (Adriamycin-Paclitaxel-Cyclophosphamide versus AC-P) as postoperative adjuvant treatment of node-positive primary breast cancer. According to the first results of this trial, dose density improves clinical outcome and sequential chemotherapy is as effective as concurrent chemotherapy. Dose dense chemotherapy may be a reasonable option for high risk node positive patients.

Dr. Piccard mentioned about the possible, new predictive marker for the selection of adjuvant treatment protocol; topoisomerase II-alpha, which is closely located to HER 2/neu on chromosome 17. A metaanalysis of HER 2/neu and topoisomerase II-alpha amplification in a number of large randomized studies comparing anthracycline-containing to CMF-type regimens may help to establish the role of these potential predictive markers.

Dr. Piccard said that, solid data were still lacking as far as optimal anthracycline (A), optimal regimen (2 or 3 drug) and optimal number of cycles (4 or 6). Up to now we do not have a level I evidence about the incorporation of taxanes (T) into A-based regimens. Careful assessment of short-term and long-term risks of T-based adjuvant therapy is still ongoing. About 50.000 women are still in the ongoing trials.

Dr. Orecchia from Milan, Italy, gave a lecture on the intraoperative radiotherapy with electrons (ELIOT) during breast conserving surgery. Dr. Streeter from U.S.A., explained the Mammosite radiation therapy system: In this system, treatment begins two to three days after surgery, and can be completed after only 4-5 days of twice-a day radiation therapy. These 2 methods are still experimental and can not be routinely recommended.

Pharmacological prevention studies of breast cancer are ongoing: New aromatase inhibitors, retinoids, cox-2 inhibitors and lower doses of tamoxifen are tested in these trials.

This year 1st St. Gallen Breast Cancer Golden Awards were given to Dr. Gianni Bonadonna and Dr. Bernard Fischer for the scientific works on the adjuvant treatment of breast carcinoma.

International consensus panel was made at the last day of the conference. There were 25 participants; 1 pathologist, 1 radiation oncologist, 2 epidemiologists, 5 surgeons and 16 medical oncologists. Risk groups, predictive factors and treatment options (surgery, adjuvant systemic therapy and adjuvant radiation therapy) were discussed. Except for anastrozole alternative in the adjuvant treatment of postmenopausal women who have developed a complication attributable to tamoxifen (i.e., thromboembolic event, persistent vaginal bleeding), there was no difference from St. Gallen 2001. All panel members recommended to WAIT UNTIL 2005 for the ongoing clinical trials' results. Results of this panel will be published in Journal of Clinical Oncology at September 2003. The date of 9th St. Gallen Conference is 26-29 January 2005.