EORTC Study Shows LHRH-agonist Added to Tamoxifen Improves Premenopausal Patient Survival in Metastatic Breast Cancer

Combined LHRH-agonist and tamoxifen are more effective than treatment with either drug alone in premenopausal metastatic breast cancer, an EORTC study has shown.

Fourteen centres from six European countries and one from South Africa entered 161 patients into the study. The patients were equally randomised between treatment with buserelin, tamoxifen or the combination. So far, the median follow-up is 4.5 years (range 0.2–8 years). Currently, 87 patients have died, all from cancer.

Dr Jan G.M. Klijn, Head of the Division of Endocrine Oncology, Department of Medical Oncology, the Rotterdam Cancer Institute, The Netherlands, said, "Combined treatment with the LHRH agonist buserelin and tamoxifen appeared to be more effective in premenopausal metastatic breast cancer than single treatment with each drug alone with respect to response rate, progression-free survival and overall postrelapse survival."

Combined treatment did not suppress plasma oestradiol levels any more than buserelin alone. In contrast, single treatment with tamoxifen caused high blood oestradiol concentrations for years.

The objective response rate during combined treatment was 50% versus 29–33% during treatment with each drug alone. The duration of response to combined treatment and the time to treatment failure was also clearly superior to those of single treatment (nearly doubled). More importantly, so far, only 40% of the patients treated with the combination therapy have died in contrast to 63–71% of patients treated with tamoxifen or buserelin alone. The constructed actuarial survival curves show that at 5 years after start of treatment ± 45% of patients will survive after combination treatment in contrast to only ± 15% after single treatment (± 30% difference). This improved survival was observed irrespective of the organ site of metastasis.

Selection Bias in Breast Cancer Trials of High-dose Chemotherapy and Bone Marrow Transplantation

Uncontrolled trials reporting the benefits of high-dose chemotherapy and bone marrow transplantation in high-risk breast cancer may be misleading, according to results of a retrospective study in Spain. The selection criteria in uncontrolled trials favours patients that have a more favourable prognosis.

Dr Rocio Garcia-Carbonero, the Medical Oncology Hospital, Madrid, Spain, studied 267 out of a total of 2900 breast cancer patients who showed involvement of ten or more positive axillary lymph nodes. Of these, 171 received conventional chemotherapy. Of these 171, it was found that those who could have met the standard selection criteria for high-dose chemotherapy plus bone marrow transplantation actually had a better clinical outcome than those who did not.

"Our retrospective study shows that the encouraging results reported by trials of high-dose chemotherapy in high-risk breast cancer without appropriate control groups may reflect an overestimation of their actual efficacy," said Dr Garcia-Carbonero. She said this result emphasised the need for randomised controlled trials of high-dose chemotherapy before its widespread use. At least three such randomised trials are under way internationally, and their results are eagerly awaited.

EORTC Study Refutes Meta-analysis on Portal Vein Infusion in Colorectal Cancer

The largest reported trial of adjuvant portal vein infusion of 5-FU and heparin in colorectal cancer concludes that portal vein infusion (PVI) alone as adjuvant to surgery in colorectal cancer cannot be recommended.

Dr Tarek Sahmoud, senior statistician and protocol review committee co-ordinator at the EORTC commented, "In contrast to the recent meta-analysis which was based on about 4000 patients and showed a small benefit (but did not include our trial), PVI, at this dose and schedule, had no activity with respect to survival, recurrence-free survival and incidence of liver metastases."

The EORTC and The Gruppo Interdisciplinare Valutazione Interventi in Oncologica (GIVO) initiated together the current trial comparing one week continuous PVI with 5-FU 500 mg/m^2 plus heparin 5000 IU to no adjuvant treatment (control arm) in patients with colorectal cancer submitted to curative resection. 1235 patients were randomised, 619 to the control arm and 616 to the PVI arm.

Presently, the EORTC and the Swiss Group (SAKK) are investigating the value of PVI in combination with adjuvant systemic chemotherapy.