5137 POSTER

Gonadotropin-Releasing Hormone analogues (Gn-RH) in high risk premenopausal breast cancer patients (Pre-HR-BC): improved clinical outcome through immune mediated mechanisms

F. Recchia[1], G. Candeloro[1], R. Bisegna[1], S. Necozione[2], C.O.C. Recchia[3], S. Rea[4]. *[1]Azienda Ospedaliera SS Filippo e Nicola, Oncologia, Avezzano, Italy; [2]Università degli Studi, Epidemiologia Clinica, L'Aquila, Italy; [3]Azienda Ospedaliera SS Filippo e Nicola, Psicologia Oncologica, Avezzano, Italy; [4]Università degli Studi, Oncologia Chirurgica, L'Aquila, Italy*

Background: Systematic reviews have found that Gn-RH analogues are useful in the treatment of premenopausal women with early breast cancer. It has been shown that estradiol (E2) expands T regulatory cells (T-regs) and modulates vascular endothelial growth factor (VEGF) expression in breast cancer cells. For these reasons we hypothesized that the benefits of Gn-RH administration, improving the immune function and decreasing (VEGF), could extend, beyond ovarian protection.
Materials and Methods: From 05–1997 to 05–2007 180 patients with Pre-HR-BC were entered into an ovarian-protection study. At baseline, one week before chemotherapy, patients received a Gn-RH analogue which was continued for five years. Adjuvant chemotherapy was tailored to the peculiar biologic features of each patient, including cyclophosphamide, methotrexate, and 5-fluorouracil in 24 patients, an anthracycline and taxane based regimens in 156 patients (40 with positive c-erb-2 tumors). Seventeen patients with >10 positive axillary lymph nodes and 36 patients with triple negative tumors, received a platinum-based consolidation high-dose chemotherapy with or without autologous peripheral blood progenitor cell transplantation, respectively. Radiation therapy was administered to 145 patients. During the 5 years of Gn-RH administration, patients received a strong psychological support, biphosphonates, and after the end of chemotherapy, estrogen receptor positive (ER+) patients received an aromatase inhibitor.
Results: Characteristics of patients. Mean age was 42 years (range, 26−50 yrs). 69% of patients were ER+, while 31% were estrogen receptor negative (ER−). Total number of positive nodes was 479, with a mean of 2.6 for each patient. UICC stage was II in 114 women and III in 66 women. Serum E2 was suppressed to values <40 pg/mL in all patients. After LH-RH administration, a statistically significant improvement was observed in lymphocyte number ($p < 0.005$), a decrease in T-reg number ($p < 0.005$) and VEGF ($p < 0.005$) with respect to baseline values. After a median follow-up of 100 months, 10-years overall progression-free survival and overall survival rate were 83% with no difference between ER+ and ER− patients.
Conclusions: These data show that the administration of a Gn-RH analogue improves lymphocyte number, decreases T-regs and VEGF, and seems to improve the expected outcome of Pre-HR-BC patients through immunologic mechanisms.

5138 POSTER

Impact of hormonal therapy (HT) on cognitive function in postmenopausal women (PMW) with hormone receptor-positive (HR+) breast cancer (BC)

M. Untch[1], R. O'Regan[2]. *[1]Academic Hospital of the University Charite Berlin, Gynecologic Oncology and Obstetrics, Berlin, Germany; [2]Emory Winship Cancer Institute, Hematology and Medical Oncology, Atlanta, USA*

Background: Aromatase inhibitors (AIs) (anastrozole [ANA], letrozole [LET], exemestane [EXE]) are replacing tamoxifen (TAM) as a treatment of choice in HR+ PMW with early BC (EBC). Plasma estrogen suppression by HT may affect cognition, as areas of the brain involved in cognitive function (hippocampus and amygdala) are rich in estrogen receptors. Levels of estrogen are significantly lower in women on AIs vs those on TAM. Cognitive impairment may have a significant impact on medication adherence and quality of life.
Materials and Methods: Literature published in the past 5 years on cognitive functioning in women with BC treated with TAM or AIs was reviewed.
Results: The number of publications on the topic was limited. AIs or TAM appear to affect cognitive function when women with BC are compared with healthy controls (HC). However, results comparing TAM with AIs are not consistent (Table) due to various trial designs, differences in population and trial duration, and effect of prior chemotherapy. Data on LET were not available, but data from the BIG 1−98 trial on the impact of TAM vs LET on cognition will be presented at ASCO 2009.
Conclusions: Compared with HC, HT for BC impacts some aspects of cognition. The effect of ANA and EXE compared with TAM is less clear and not conclusive. To date, no long-term effect of HT on cognition has been investigated in patients with BC. Most trials are not designed to evaluate cognitive functioning, and more studies are needed. The BIG 1−98 trial will provide information on LET vs TAM.

Author	Drugs	N; Population; Duration	Findings
Bender, 2007	TAM vs ANA	N = 31; EBC PMW; ⩾3 mo	ANA < TAM on verbal and visual learning
Jenkins, 2008 (IBIS II)	ANA vs placebo (PLA)	N = 227; PMW at high risk of developing BC; 24 mo	ANA = PLA on all cognitive tasks
Hermelink, 2008	TAM and AIs	N = 101; BC patients; 1 y	No effect on cognition for TAM or AIs
Schilling, 2003	TAM, ANA vs HC (ATAC)	TAM or ANA, n = 94; HC, n = 35 EBC patients	HT = HC on working and visual memory, attention; HT < HC on verbal memory and processing speed
Schilder, 2009	TAM vs EXE vs HC	TAM (n = 30) or EXE (n = 50) vs HC (n = 48); PMW with BC; 2 y	TAM = EXE < HC on verbal fluency and information processing speed; TAM < EXE on verbal functioning; EXE < TAM on manual motor speed
Jones, 2003	TAM vs EXE (TEAM)	N = 499; 12 mo	EXE = TAM on impaired word finding

5139 POSTER

Patterns of care in postmenopausal early breast cancer patients participating in the TEAM (Tamoxifen Exemestane Adjuvant Multinational) study: variations in locoregional therapy between different countries

J.G.H. van Nes[1], C. Seynaeve[2], S. Jones[3], A. Hasenburg[4], D.W. Rea[5], J.M. Vannetzel[6], L. Dirix[7], C. Markopoulos[8], W.M. Meershoek-Klein Kranenbarg[9], C.J.H. van de Velde[1]. *[1]Leiden University Medical Centre, Surgery, Leiden, The Netherlands; [2]Erasmus Medical Centre-Daniel den Hoed Cancer Centre, Medical Oncology, Rotterdam, The Netherlands; [3]Erasmus Medical Centre-US Oncology Research, Oncology, Houston Texas, USA; [4]University Hospital Freiburg, Obstetrics and Gynecology, Freiburg, Germany; [5]University of Birmingham, Division of cancer studies, Birmingham, United Kingdom; [6]Institut du Sein Henri Hartmann Clinique Hartmann, Gynecology, Neuilly, France; [7]AZ Sint-Augustinus, medical oncology, Antwerp, Belgium; [8]Athens University Medical School, Breast Unit, Athens, Greece; [9]Leiden University Medical Centre, Datacentre, Leiden, The Netherlands*

Background: The Tamoxifen Exemestane Adjuvant Multinational (TEAM) trial is an international randomized trial evaluating the efficacy and safety of exemestane, alone or in sequence following tamoxifen. The large number of included patients offered the opportunity to explore the locoregional treatment practices between countries.
Material and Methods: Patients were enrolled in Belgium, France, Germany, Greece, Ireland, Japan, the Netherlands, UK and the USA. There was a generally accepted core protocol with minor differences in eligibility criteria between countries reflecting variations in national guidelines and practice patterns regarding adjuvant endocrine therapy. All data were analysed using the statistical package SPSS for Windows 15.0. Pearson's chi-square test was used to compare frequencies between groups. Univariate and multivariate analyses were performed using logistic regression procedure to determine factors with impact on differences.
Results: Between 2001 and 2006, 9779 patients were randomised. Baseline characteristics and ranges by country were: mean age: 64 years (SD 9.0); tumour size T1: 58% (range 37−76%, $p < 0.001$); positive nodal status: 47% (range 26−85%, $p < 0.001$). A mastectomy was performed in 44% of patients, ranging from 19% in France to 56% in the Netherlands ($p < 0.001$). Independent factors for type of breast surgery were country, age, tumour size and calendar year of surgery. Radiotherapy after breast conserving surgery (BCS) was given in 93% of patients, being 100% in France and Belgium, while up to 13−14% of patients from Japan, the UK/Ireland and the USA did not receive radiotherapy in this setting. An axillary lymph node dissection (ALND) was performed in 82% of patients, ranging from 75% in the USA to 99% in the UK/Ireland. In multivariate logistic regression analysis, country, type and year of breast surgery were independent factors associated with ALND.
Conclusions: Despite international consensus guidelines, wide global variations concerning locoregional treatment practices of early breast cancer are observed among different countries, requiring further research and efforts to achieve optimal local treatment for each breast cancer patient.