PO100

A HOSPITAL-BASED STUDY OF FACTORS RELATED TO LATE STAGE DIAGNOSIS IN A SERIES OF 44,085 BREAST CANCER PATIENTS IN BRAZIL

Luiz Claudio Thuler [1,2], Anke Bergmann [1,3], Letícia Casado [1]
[1] *Brazilian National Cancer Institute (INCA), Rio de Janeiro, Brazil*
[2] *Federal University of Rio de Janeiro State (UNIRIO), Rio de Janeiro, Brazil*
[3] *Centro Universitário Augusto Motta (UNISUAM), Rio de Janeiro, Brazil*

Introduction: Significant advances in the prevention, diagnosis and management of breast cancer have been made in recent years. However, breast cancer remains a complex disease affecting millions worldwide. In Brazil, the majority of women tend to be diagnosed at a more advanced stage of disease.
Objective: The aim of this study was to examine the factors related to late stage diagnosis in a series of patients with breast cancer registered in a searchable database produced by the Brazilian National Cancer Institute (INCA).
Material and Methods: The IntegradorRHC, a public-domain program, collects uniformly reported data on patient demographics, year of diagnosis, tumor characteristics, and treatment utilization for cancers patients. Presently 145 hospital-based cancer registries, from 88 Brazilian municipalities, participate. It comprises more than 500,000 cancer cases. A total of 71,476 patients with breast cancer diagnosed as their first primary malignancy between 2000 and 2009 were identified. We excluded 13,985 patients who were first diagnosed and receive all of first course of therapy at another institution, or were diagnosed at autopsy or by death certificate only (non-analytic cases) and 13,406 cases with missing information, leaving 44,085 patients in the final analyses. Data included epidemiological, socio-demographic and clinical factors. Chi-square and odds ratio were performed to examine associations between studied factors and late stage diagnosis (stages IIB to IVB). Statistical analysis was carried out using EpiInfo version 6.
Results: The mean age was 55.68 years, with a considerable female preponderance in gender distribution (99.05%). Sixty percent had advanced disease ($\geq$II B). The results suggest that being female (OR= 2.28; 95% CI 1.87-2.79; $p<0.001$), age 20-49 (OR= 1.23; 95% CI 1.18-1.28; $p<0.001$), black (OR= 1.79; 95%CI 1.65-1.94; $p<0.001$) or mulatto (OR= 1.53; 95% CI 1.46-1.60; $p<0.001$), single/separated/divorced/ widowed (OR= 1.15; IC95% 1.11-1.20; $p<0.001$), diagnosed between 2000 and 2005 (OR= 1.09; 95%CI 1.05-1.14; $p<0.001$), current smoker (OR= 1.12; 95%CI 1.06-1.18; $p<0.001$), treated in a hospital located in the Northeast Region of Brazil (OR= 1.33; 95%CI 1.27-1.39; $p<0.001$), having less than 8 years of formal education (OR= 1.41; 95%CI 1.34-1.47; $p<0.001$) or ductal infiltrant carcinoma (OR= 1.69; 95%CI 1.61-1.77; $p<0.001$) were more likely to be diagnosed at a late stage. No relationship could be established between alcohol consumption ($p= 0.87$) and breast cancer stage.
Conclusion: In summary, our study has identified several factors that if addressed could reduce the number of advanced stage breast cancer cases. The results have important implications in public policy. Targeted education and policies could reduce the burden of this disease.

PO101

RESPONSE TO SUBSEQUENT ENDOCRINE THERAPY IN PATIENTS TREATED WITH FULVESTRANT 500MG OR ANASTROZOLE: RESULTS FROM FIRST

John F.R. Robertson [1], Justin P.O. Lindemann [2], Sally Garnett [2], Antonio Llombart-Cussac [3], Janusz Rolski [4], David Feltl [5], John Dewar [6], Matthew J. Ellis [7]
[1] *Division of Breast Surgery, University of Nottingham, Nottingham, UK*
[2] *AstraZeneca Pharmaceuticals, Macclesfield, UK*
[3] *Hospital Arnau de Vilanova, Lérida, Spain*
[4] *Centrum Onkologii, Instytut im M. Sklodowskiej-Curie, Krakow, Poland*
[5] *FNsP Ostrava, Radioterapeutická klinika, Ostrava-Poruba, Czech Republic*
[6] *Department of Oncology, Ninewells Hospital and Medical School, Dundee, UK*
[7] *Washington University School of Medicine, St Louis, USA*

Background: The Fulvestrant fIRst-line Study comparing endocrine Treatments (FIRST) compared fulvestrant 500mg with anastrozole as first-line endocrine therapy in postmenopausal women with hormone receptor-positive (HR+) advanced breast cancer. Fulvestrant 500mg was at least as effective as anastrozole in terms of clinical benefit rate (CBR; primary study endpoint) and objective response rate (ORR); however, time to progression (TTP) was significantly longer with fulvestrant 500mg. We present an analysis of response to subsequent breast cancer therapy.
Methods: FIRST is a Phase II, randomised, open-label, multicentre study comparing fulvestrant 500mg (500mg/month plus 500mg on Day 14 of Month 1) with anastrozole (1mg/day) as first-line endocrine therapy in postmenopausal women with advanced breast cancer. Following withdrawal from randomised treatment, best overall response (complete response [CR], partial response [PR], stable disease [SD] $\geq$24 weeks, SD $<$24 weeks, not evaluable, or progressive disease) to first subsequent systemic breast cancer therapy was determined by investigator opinion. ORR is the proportion of patients with a best overall response of CR or PR. CBR is defined as ORR plus SD $\geq$24 weeks.
Results: In total, 205 patients received fulvestrant 500mg (n=102) or anastrozole (n=103). At data cut-off for the follow-up analysis for TTP, 63 patients in the fulvestrant 500mg group and 79 patients in the anastrozole group had progressed. Median TTP was 23.4 months for fulvestrant 500mg and 13.1 months for anastrozole (hazard ratio 0.66; 95% confidence interval, 0.47-0.92; p=0.01). The number of treatment failures was 76 in the fulvestrant 500mg group and 87 in the anastrozole group.
A total of 64 (62.7%) patients in the fulvestrant 500mg group and 69 (67.0%) patients in the anastrozole group received subsequent systemic therapy for breast cancer (chemotherapy, endocrine therapy, novel targeted therapy or unknown). ORR to subsequent therapy was 23.4% (15/64 patients) in the fulvestrant 500mg group and 21.7% (15/69 patients) in the anastrozole group. CBR to subsequent therapy was 43.8% (28/64 patients) and 46.4% (32/69 patients) in the fulvestrant 500mg and anastrozole groups, respectively. Endocrine therapy was received by 34 (53.1%) patients in the fulvestrant 500mg group and 50 (72.5%) patients in the anastrozole group (most common endocrine therapies: anastrozole and letrozole in the fulvestrant 500mg group; fulvestrant and exemestane in the anastrozole group). Of those patients who received subsequent endocrine therapy, ORR was 8.8% (3/34 patients) for fulvestrant 500mg and 14.0% (7/50 patients) for anastrozole. CBR was 41.2% (14/34 patients) for fulvestrant 500mg and 42.0% (21/50 patients) for anastrozole.
Conclusion: Patients who progress on either fulvestrant 500mg or anastrozole as first-line treatment for HR+ advanced breast cancer may experience comparable CBRs to first subsequent endocrine therapy.

PO102

BENEFIT OF CONTINUING TRASTUZUMAB BEYOND PROGRESSION IN HER2-POSITIVE METASTATIC BREAST CANCER (MBC) IS INDEPENDENT OF THE CHEMOTHERAPY PARTNER: MESSAGE FROM A SINGLE-CENTRE RETROSPECTIVE STUDY.

Raffaella Palumbo, Federico Sottotetti, Antonio Bernardo, Maria Rosa Strada, Alberto Riccardi, Cristina Teragni, Barbara Tagliaferri, Giovanni Bernardo
Fondazione Maugeri-IRCCS, Pavia, Italy

Background: The activity of trastuzumab-based chemotherapy (CT) in HER2-positive MBC is now well-established, but the question of the optimal antineoplastic partner remains a relevant issue. We performed a retrospective comparison of the clinical outcomes associated with different trastuzumab-CT combinations.
Patients and methods: Patients for this analysis were selected from a monoinstitutional database containing the data of women with HER2-positive MBC (IHC3+ or FISH positive) receiving first-line trastuzumab-based CT between February 2005 and December 2008. Treatment activity was assessed according to the WHO criteria, time to progression (TTP) and overall survival (OS) were calculated by the Kaplan Meier method (intent-to-treat analysis).
Results: A total of 147 women with measurable disease were evaluated: 57 received trastuzumab with weekly vinorelbine (25 mg/m^2 until tumor

progression), 48 trastuzumab plus docetaxel (75-100 mg/m^2 every 3 weeks for 6-8 cycles), 42 a triple combination of three-weekly trastuzumab plus oral vinorelbine (60mg/m^2 days 1 and 8 q 21) and capecitabine (1000 mg/m^2 bid days 1->14, every 3 weeks). Response rate (RR) was 76% in trastuzumab+vinorelbine group, 68% in the docetaxel-based regimen and 72% in the triple combination. More treatment-related grade 3-4 toxicities were recorded in the docetaxel-treated population. Median follow-up was 41.2 months, median duration of trastuzumab-based therapy was 18.2 months. Following disease progression, all women continued trastuzumab-based CT as second-line or subsequent lines of treatment, shifting the chemotherapeutic partner, according to our institution policy: 142 as 2nd line treatment, 69 as 3rd , 48 as 4th and 16 as 5th. There was no significant difference in median TTP according to 1st-line treatment type (14, 11 and 12 months, respectively, p=0.62), while a slow decline was observed throughout the successive CT lines, with almost stable values beyond the 3rd (7.5 e 7.2, respectively). Median OS from the start of trastuzumab therapy was 36, 32 and 34 months, respectively, in the 3 treatment group (p=0.48). In multivariate analysis the number of trastuzumab-based regimens was significantly correlated to OS (p=0.02), while no correlation was found between the survival benefit and the different type of CT.

Conclusions: Our results confirm that the benefit of continuing trastuzumab beyond progression was independent from the CT partner, also suggesting a benefit in overall clinical outcome for given subsequent lines of trastuzumab-based therapy at the time of disease relapse.

PO103

METRONOMIC ORAL COMBINATION CHEMOTHERAPY WITH CAPECITABINE AND CYCLOPHOSPHAMIDE IN PATIENTS WITH METASTATIC BREAST CANCER: A SINGLE INSTITUTION EXPERIENCE

Shintaro Takao, Kaori Tane, Kouichi Hirokaga, Youko Maekawa
Hyogo Cancer Center, Akashi, Japan

Background: Metronomic combination chemotherapy with the oral capecitabine (X) combined with oral cyclophosphamide (C) has showed promising efficacy without significant toxicity in three phase II studies. We widely used this XC regimen for the patients with metastatic breast cancer (MBC) in our institution by two reasons. First, the patients prefer oral, home-based therapy to IV hospital-based therapy. Second, there is an established scientific rationale for XC regimen. Capecitabine is converted to 5-FU in the presence of thymidine phosphorylase (TP). TP, presented at significantly higher concentrations in the tumor than in other tissues, is upregulated by cyclophosphamide. A synergistic effect was observed with the XC combination. We conducted a retrospective study to evaluate an all-oral XC combination in patients with MBC in Hyogo Cancer center.

Material and methods: We retrospectively evaluated 56 patients (median age 62; range 32-82 years) with metastatic breast cancer. The patients received X 828 mg/m^2 with 65 mg/m^2/day C, days 1–14 every 3 weeks.

Results: Median cycles of XC treatment were six (range 1-32 cycles). Twenty-four patients received XC more than 8 cycles. The overall response rate (ORR) was 41.1% (95%CI: 28.1–55.0%). In a further 21.4%, disease was stabilized for ≥24 weeks (LSD), resulting in a clinical benefit response rate (CBR) of 62.5% (95%CI: 48.6–75.1%). A subanalysis of efficacy accoding to number of prior chemotherapy regimens for MBC showed that the patients with no prior chemotherapy presented ORR of 52.6% and CBR of 73.7%. ORR and CBR of the patients with one prior chemotherapy resulted in 35.3% and 58.8%, while those with more than two prior chemotherapy and 35.0% and 55.0%, respectively. Of 22 patients pretreated with capecitabine, we observed one CR, 5PRs (ORR 27.3%) and 5 patients with LSD (CBR50%) with XC therapy. Median progression free survival (PFS) and overall survival (OS) was 7.0 months (95% CI: 6.9–11.5months) and 13.8 months (95% CI: 14.1–19.6months), respectively. Subpopulation analysis demonstrated median PFS of 7.0 months in estrogen-receptor positive, 7.3 months in triple-negative disease and 6.8 months in HER2-positive disease. The 1-year PFS rate and OS rate was 32.4% and 72.8%, respectively. Toxicity was generally mild. Grade 3 adverse events comprised 9 leukopenia (16%), 1 thrombocytopenia (2%) and 1 hand-foot syndrome (2%).

Conclusions: Oral XC combination chemotherapy is an effective therapy for MBC, demonstrating high activity in any subtype with few severe side effects. This metronomic chemotherapy could be beneficial for the patients with MBC who have been treated with capecitabine, and further evaluation is justified.

PO104

STUDY OF MUTATIONS IN BRCA1 AND BRCA 2 GENE AMONG THE BREAST CANCER PATIENTS IN EASTERN INDIAN POPULATION.

Abhijit Chakraborty, Deboshree Bhattacharyya (Majumdar), Jayasri Basak, Ashis Mukhopadhyay
Netaji Subhas Chandra Bosr Cancer Research Institute, Kolkata, W.B, India

Background: Breast Cancer is the most commonly diagnosed cancer among Indian women. A large number of distinct mutations in the BRCA1 and BRCA2 genes have been reported worldwide, In West Bengal (India) till date no such supporting data of BRCA1 and BRCA 2 gene causing mutations are available. From our hospital record we have observed that there are many breast cancer patients whose molecular level diagnosis and family level survey has not yet been done.

Objectives: 1. To detect BRCA1 and BRCA2 mutations of patients with breast and ovarian cancer and their 1st& 2nd degree relatives in their families.
2. To study BRCA1 & BRCA2 gene expression in normal individuals as control.
3. To establish a genetic profile for the studied population.
4. To study the BRCA1 & BRCA2 gene positivity as prognostic factor in Breast Cancer patients.
5. Analysis of haplotype pattern linked with BRCA1 and BRCA 2 mutations

Methods: Firstly to make aware the individual and its family about the familial inheritance of breast cancer. Then cases were selected with regards to early onset of disease (<45 yrs) and family history of breast and ovarian cancer. Out of 150 patients with family history (83 individuals) and without family history (67 individuals) were screened. 70 control subjects were used to analyze the mutation. We used multiplex PCR, PCR-SSCP and direct sequencing for screening. Products with abnormal patterns in SSCP were sequenced to identify the mutation.

Results: Mutations were identified in 48 families (32%); 37 had BRCA1 mutation and 11 had BRCA2 mutation. In case of BRCA1 and BRCA2 gene, insertion, deletion, intronic variants were identified. In most cases of BRCA1 mutation 185delAG (14 of 37) and 5382 InsC (9 of 37) mutations was found. Significantly fewer BRCA2 mutations (2 of 11) detected in families with ovarian cancer families. 1 family had male breast cancer with BRCA1 mutation.

Conclusion: BRCA1 mutations were more prevalent than BRCA2 mutation. Breast Cancer diagnosis before age 50, Breast and ovarian cancer in single individuals are significantly more common in BRCA 1 & 2 mutation.

Reference: Saxena S et al Clinico-morphological patterns of breast cancer including family history in a New Delhi hospital, India – a cross-sectional study. World J Surg Oncol 2005, 3:67
Lynch HT et al. 'Breast cancer family history as a risk factor for early onset breast cancer.' Breast Cancer Res Treat 1988;11:263–7
Choi D.H, Lee M.H, et al Incidence of BRCA1 and BRCA2 Mutations in Young Korean Breast Cancer Patients", Journal Of Clinical Oncology, 2004 ;22 (9)
Dufoth R.M, Carvalho S, etalAnalysis of BRCA1 and BRCA2 mutations in Brazilian breast cancer patients with positive family history Sao Paulo Med J. 2005;123(4):192-7.

PO105

THE VERTICAL RECTUS ABDOMINIS MYOCUTANEOUS (VRAM) FLAP IS THE PREFERRED MEANS OF POST-MASTECTOMY DEFECT COVER FOR LARGE BREAST TUMOURS

Tse Han Loong, Yia Swam Tan, Ern Yu Tan, Juliana Chen, Marcus Wong, Mun Yew Patrick Chan
Tan Tock Seng Hospital, Singapore, Singapore