Wednesday, 24 March 2010 15:00–17:00

KEYNOTE SYMPOSIUM

Partnership for the fight against breast cancer

1 Invited

Specialist Breast Units − The patient advocate perspective

E. Verschuur[1], C. Murphy-Whyte[2]. [1]*Europa Donna, President;* [2]*Europa Donna, Vice-President*

The quality of breast cancer care that European women receive today differs from country to country and from region to region. This is despite the evidence that the most effective means of reducing disparities in care and mortality are through population based mammography screening programmes and the setting up of specialist breast units combining audit with good practice standards.

Women, advocates, politicians and policy makers need to know what high quality breast care services to expect, demand and implement.

The keynote address will trace the role of EUROPA DONNA in the development and promotion of the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis which were created with input from top European Cancer Organisation's and are EUROPA DONNA's reference document for benchmarking and best practice.

The experience of the patient advocate in helping women, advocates and politicians work together to ensure that the best breast cancer services are available to women wherever they live will be explored.

By looking at the patient care pathway from referral to diagnosis and treatment, the key features of specialist breast units from the patient perspective will be considered as well as the quality of the patient experience. Particular attention will be given to the importance of good communication throughout the patient's pathway of care and on ways to improve communication and collaboration with multi-disciplinary team members at each stage of diagnosis, treatment and aftercare to accomplish the best outcome.

2 Invited

EUSOMA − Achieving the critical practice

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Following the EBCC-Florence, -Brussels and -Barcelona Statements, Eusoma has been committed in making available for women in Europe a high quality specialist Breast Service.

To achieve this aim Eusoma has defined the requirements of a specialist breast unit, the standards for the training of specialized health professionals dealing with breast cancer and a set of recommendation for breast cancer diagnosis and care. Moreover Eusoma has developed a certification process and an audit system to evaluate if units comply with what defined by Eusoma, to make recognizable to patients, practitioners and health authorities Units providing such a service of being of high quality.

The seven basic criteria for a breast unit are:

- A single integrated Unit
- Sufficient cases to allow effective working and continuing expertise
- Care by breast specialists in all the required disciplines
- Working in multidisciplinary fashion in all areas
- Providing all the services necessary − from genetics and prevention, through the treatment of the primary tumour, to care of advanced disease and palliation
- Patient support
- Data collection

Breast Units are mostly established in medium size hospitals, working in a functional way. These Units are encouraged to provide research opportunities. However, with regard to health professionals, some critical points have to be taken into account:

– Burn out in terms of emotional exhaustion, depersonalization, career satisfaction
– Lack of homogeneity in the training of specialized health professionals
– Lack of recognized specialization in the different disciplines at national level
– The need to set up training program for highly specialized health professionals within the University at national level

5 Invited

Partnership approach to clinical research in the UK

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The opportunity to participate in a clinical trial should be an option for all women with breast cancer. This has been shown to lead to an improved level of personalised care, enable access to potentially useful new treatments and provide the opportunity to help the patients of the future. However, this requires both a comprehensive national research infrastructure as well as a broad portfolio of trials to cover the many clinical and biological settings encountered in breast cancer care.

In the UK, a partnership known as the National Cancer Research Network (NCRN) was established between the National Health Service, the major cancer charities and research funders in 2001. The NCRN has provided funding on a population basis to all cancer networks across the UK to establish a dedicated research workforce to support cancer clinicians and patients. In addition, the National Cancer Research Initiative (NCRI) oversees research activity and has established site-specific groups to develop the trial portfolio including the Breast Cancer Study Group (BCSG).

Since 2001 more than 36,000 breast cancer patients have been included in nationally approved randomised clinical trials (RCTs), many of them practice changing. In addition, over 65,000 patients have participated in other non-randomised studies including biomarker discovery, genetic epidemiology, supportive care and lifestyle issues. There are currently 52 academic NIHR breast cancer trials open to accrual across the entire spectrum of the disease. 9.1% of incident cases were recruited to a RCT in 08/09, an absolute increase of 0.6% over the previous year. 11,540 patients were included in non-randomised studies. In total, research activity approximates to one third of all incident cases. The vast majority of trials also incorporate a translational component. This has resulted in an extensive tumour and biomarker sample bank to help our understanding of the complex interactions between treatments and tumour biology. Additionally the research infrastructure of the NCRN has enabled successful partnership with more than 30 pharmaceutical companies and delivery on a broad range of industry sponsored studies.

Wednesday, 24 March 2010 18:15–19:15

POSTER SESSION

Adjuvant treatment of breast cancer

7 Poster discussion

Outcomes of women with early stage HER-2 over-expressing breast cancer receiving adjuvant trastuzumab: a population based analysis

S. Chia[1], C. Speers[2], K. Gelmon[1], S. Ellard[3], R. Pickering[4], S. O'Reilly[1], M. Seal[1]. [1]*BC Cancer Agency, Medical Oncology, Vancouver BC, Canada;* [2]*BC Cancer Agency, Breast Cancer Outcomes Unit, Vancouver BC, Canada;* [3]*BC Cancer Agency, Medical Oncology, Kelowna BC, Canada;* [4]*BC Cancer Agency, Pharmacy, Vancouver BC, Canada*

Background: Large randomized trials assessing the benefit of adjuvant trastuzumab in early stage HER2+ breast cancer have demonstrated a 50% reduction in disease recurrence and a 30% improvement in survival. The objective of this study was to describe the utilization and outcomes of women who received adjuvant trastuzumab (T) for HER-2 positive breast cancer in British Columbia since publicly funded population based use was initiated in July 2005.

Methods: Women with stage I-III breast cancer positive for HER-2 over-expression by immunohistochemistry (3+) or by fluorescence-in-situ hybridization (ratio $\geqslant$2.0) diagnosed from July 2004 to December 2006 were included in this study. A search of the BCCA Breast Cancer Outcomes Unit database revealed demographic information, tumour characteristics and outcomes on all identified patients. Cases were matched with the provincial BCCA pharmacy data repository to determine the proportion of women who received adjuvant T and to differentiate groups according to type of systemic treatment.

Results: 704 HER-2 positive patients were identified in this study. 68% (n = 480) received T. Nearly 100% of patients receiving adjuvant T underwent chemotherapy versus 27% of patients who did not receive T (n = 224). The majority of patients received T in a concurrent manner (71%) versus sequential therapy (29%). Median follow-up was 2.1 years.

Two-year RFS in patients receiving trastuzumab was 95.9% (95% CI, 93.4–97.5) and OS was 99.3% (95% CI, 97.9–99.8). First site of distant

metastases was brain in 17.8% of relapsing patients (35% of relapsing patients who received T). The 2 year RFS among patients receiving concurrent chemotherapy + T was 94.7% whereas sequential CT followed by T was 98.4%. In the T treated cohort the 2 year RFS among node negative and node positive patients were 97.8% and 94.4% respectively (p = 0.06). In the cohort of HER-2 positive patients who did not receive T, the 2 year RFS among node negative and node positive patients were 90.7% and 75.5% respectively (p = 0.007). The corresponding 2 year distant RFS in this same cohort was 93.1% and 80.3% respectively (p = 0.01).

Conclusions: A population based analysis of adjuvant trastuzumab use among Canadian women demonstrates highly favorable outcomes at the 2 year follow-up period. Although retrospective in nature, this is one of the first studies to observe breast cancer outcomes in a more generalized population with widespread publicly funded use of T.

8 Poster discussion

Independent prognostic factors for response: updated results of the ABCSG-24 study evaluating the addition of capecitabine to epirubicin-docetaxel neoadjuvant therapy for early breast cancer (EBC)

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Background: The randomised, phase III ABCSG-24 study evaluated the influence of the addition of capecitabine (C) to 6 cycles of neoadjuvant epirubicin-docetaxel (ED; EDC therapy) on pathological complete response (pCR) rate in patients with EBC. Additional objectives were comparison of the rates of breast conservation (BCR) and axillary lymph node involvement at the time of final surgery. The aim of the current analysis was to assess the role of known risk factors on response to EDC.

Methods: Patients with biopsy proven, operable breast cancer (except T4d), +/− nodal involvement, who were scheduled for neoadjuvant chemotherapy were stratified according to known risk factors (menopausal status, hormone receptor status, tumour grade and stage, HER2 status) and randomised to 6 x ED every 21 days (day 1: E 75 mg/m^2 i.v., D 75 mg/m^2 i.v., day 2: pegfilgrastim 6 mg) +/− C (2 × 1,000 mg/m^2/day for 14 days). The accrual target was 536 patients (94 with HER2-positive disease) to achieve 510 evaluable patients and detect a difference in the rate of pCR of 16% (ED) versus 27% (EDC) with a power of 83% at a significance level of 0.05 (two-sided Chi-squared test). Patients with HER2-positive disease were also randomised to neoadjuvant trastuzumab (T) or placebo.

Results: Baseline characteristics were well balanced between the ED (n = 257) and EDC (n = 255) groups. Median age was 49 years (range 25−73) and 67% and 74% of patients had hormone receptor-negative and HER2-negative tumours, respectively. pCR rate was significantly increased with EDC compared with ED (24.3% vs 16.0%; HR 0.58 [0.38–0.92], p = 0.02). A logistic regression model demonstrated that hormone receptor status (p < 0.001), tumour stage (p = 0.002) grade (p < 0.001), and C therapy (p = 0.03) were independent prognostic factors for pCR. Overall, no significant difference in BCR or rate of axillary lymph node involvement was noted. There was no significant difference in the incidence of serious adverse events (EDC 26% vs ED 21%) and 96% and 94% of patients receiving ED and EDC, respectively, completed all 6 cycles of therapy.

Conclusions: These data indicate that hormone receptor status, tumour stage and grade, and treatment with C are independent prognostic factors for response when C is integrated into a taxane-/anthracycline-based neoadjuvant regimen.

9 Poster discussion

Breast-conserving surgery after preoperative endocrine therapy versus chemotherapy in postmenopausal patients with estrogen-receptor-positive breast cancer

V.F. Semiglazov[1], V.V. Semiglazov[1], G.A. Dashyan[1], A.G. Manikhas[2], E.K. Ziltsova[1], A.A. Malodusheva[1], V.G. Ivanov[1], R.V. Donskih[1], R.M. Paltuev[1], A.E. Kletsel[3]. *[1]N.N. Petrov Scientific Research Institute of Oncology, Breast Cancer, St-Petersburg, Russian Federation; [2]City Oncological Hospital, Breast Cancer, St-Petersburg, Russian Federation; [3]Hospital Gross-Umstadt, Breast Cancer, Frankfurt-Main, Germany*

Background: Neoadjuvant therapy may increase the proportion of women eligible for beast-conserving surgery (BCS) by reducing tumor size. Endocrine therapy and chemotherapy have been investigated in this setting.

Methods: A total of 239 patients (pts) with ER-positive and/or PgR-positive breast cancer (T2N1−2, T3N0−1, T4N0M0) were randomly assigned to receive neoadjuvant endocrine therapy (ET) [anastrazole 1 mg/day or exemestane 25 mg/day for 3 months, 121 patients] or chemotherapy (CT) [doxorubicin 60 mg/m^2 with paclitaxel 200 mg/m^2, four 3-week cycles, 118 patients]. All pts were considered to be ineligible for BCS at enrollment. After BCS all pts received radiotherapy (50 Gy in 25 fractions). The median follow-up time was 5.6 years.

Results: The primary efficacy end point was already reported (Cancer 2007; 110: 244−54). Overall response (OR=CR+PR) was similar in the ET group (65.5%) compared with CT (63.6%; p > 0.5).

After completing neoadjuvant treatment, 31 (13%) patients did not undergo surgery: 12.3% of pts who were receiving ET and 13.5% of pts who were receiving CT. Progressive disease was observed in 9% of pts who were receiving ET and 9% of pts who were receiving CT (p > 0.5). There was a trend toward higher overall rates of objective response (OR) and BCS among patients with tumors expressing high levels of ER (Allred score >6) in the ET group compared CT (p = 0.054; 43% vs 24% respectively). There was no significant difference between ET and CT relative to the incidence of locoregional recurrences and distant metastases (7.9% and 7.3%, p = 0.99; 14.8% and 15.2%, p = 0.83, respectively).

There was no significant difference in DFS through 5 years of follow up between the 121 pts who received neoadjuvant ET and 118 women who received CT: 71.0% and 67.7% (p > 0.5).

Fifty one (43%) pts who were receiving CT experienced neutropenia (grade 2−4) that led to treatment interruption. ET was well tolerated.

Conclusion: For elderly postmenopausal women with comorbid conditions and large hormone-responsive tumors (ER+ or PgR+) BCS may be possible after well-tolerated, preoperative ET with aromatase inhibitors less toxic than CT.

10 Poster discussion

Homologous recombination deficiency in breast cancer and association with response to neo-adjuvant chemotherapy

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Background: Tumors with homologous recombination deficiency (HRD) are highly sensitive to DNA double strand break (DSBs) inducing agents, including alkylating agents and poly (ADP-ribose) polymerase (PARP)-inhibitors. BRCA1- and BRCA2- associated tumors, which are thought to be HRD, may be identifiable employing an array Comparative Genomic Hybridization (aCGH) classifier. As this classifier was primarily developed to recognize breast cancers in BRCA mutation carriers, we determined these profiles together with several other HRD characteristics in sporadic cancer patients and correlated the presence to neoadjuvant treatment response to DSB inducing chemotherapy.

Material and Methods: Forty-three triple negative (TN) and 91 estrogen receptor positive/HER2− (ER+/HER2−) pre-treatment biopsies were examined, procured from sporadic breast cancer patients scheduled to receive neoadjuvant therapy with doxorubicin/cyclophosphamide. aCGH for assessing BRCA1-like and BRCA2-like profiles was performed. In addition, BRCA1 promotor methylation, BRCA1 mRNA expression and amplification of the EMSY gene were assessed. Response to neoadjuvant treatment was assessed by measuring pathological complete remission (pCR) and near pCR at the time of surgery.

Results: Inactivation of BRCA1 was frequent in TN tumors: 54% of these tumors showed a 'BRCA1-like' profile at aCGH. BRCA1 promotor methylation and reduced BRCA1 mRNA expression were observed in 25% and 43% of the TN tumors, respectively. Although a slightly higher treatment response was seen in TN tumors with a BRCA1-like profile, this was not significant (70% vs. 42%, p = 0.231). In ER+ tumors, a BRCA2-like profile and the amplification of the BRCA2 inhibiting gene EMSY were frequently observed (37% and 15% respectively). A BRCA2-like profile was associated with a significantly higher response rate (35% vs 12%, p = 0.033). EMSY amplification and a BRCA2-like profile occurred together in only one case. EMSY was not associated with treatment response, questioning the role of EMSY in HRD.

Conclusion: Abnormalities associated with BRCA1 inactivation are present in about half of the TN breast cancers and may identify tumors that are sensitive to chemotherapy that causes DNA DSBs. In ER+/HER2− tumors, the BRCA2-like profile may indicate HRD and thus be predictive for benefit from new targeted agents, involved in DNA repair. After validation